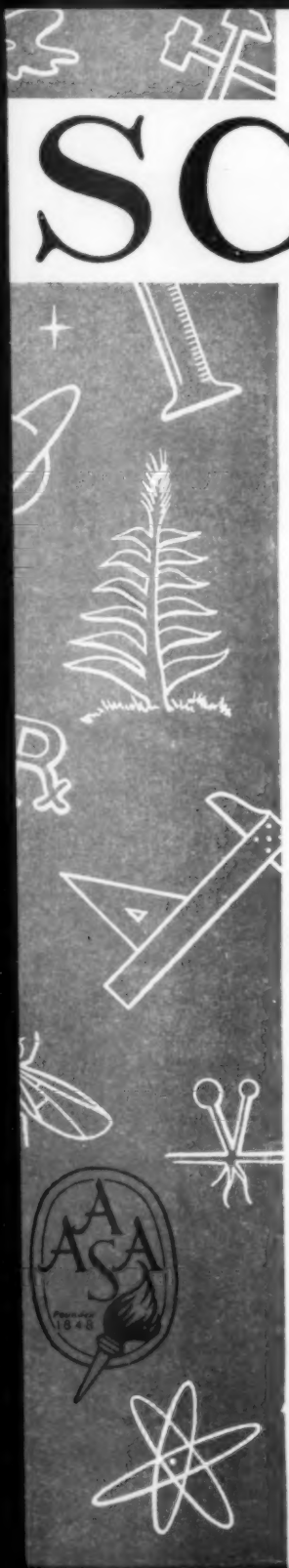

SCIENCE

NOVEMBER 14, 1952

VOLUME 116 NUMBER 3020

Contents

National Academy of Sciences: *Abstracts of Papers Presented at the Autumn Meeting, November 10–12, 1952* ____ 515

News and Notes ____ 532

Technical Papers

The Effect of 2-Aminofluorene on the Utilization of S^{35} DL-Methionine: *A. W. Wase, J. B. Allison,* and *J. F. Migliarese* ____ 536

On the Anomaly in the Heat Capacity of Manganous Oxide: *Roald K. Wangsness* ____ 537

Ammoniated Dentifrices and Hamster Caries: Further Studies on the Effects of Ingestion: *David F. Mitchell, Edith Zak Helman,* and *Dwight S. Chernausek* ____ 537

Histochemical Demonstration of Aryl Sulfatase: *Alexander M. Rutenburg, Richard B. Cohen,* and *Arnold M. Seligman* ____ 539

The Destruction of Epinephrine by the DOPA-Oxidase System of Ocular Tissue: *Winifred J. Angenent* and *George B. Koelle* ____ 543

The Effect of Ultraviolet Radiation on Sulfhydryl and Disulfide Containing Amino Acids: *Klaus Schocken* ____ 544

Comments and Communications

Relis B. Brown, Department of State, and *Francis Hemming* ____ 546

Book Reviews

The Physical Chemistry of Surface Films; Progress in Biophysics and Biophysical Chemistry; International Review of Cytology ____ 548

Association Affairs

Symposia at the St. Louis Meeting: *Raymond L. Taylor* ____ 550

Microphysiology ____ 3

Publications Received ____ 16

Meetings & Conferences ____ 18

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Microphysiology

IF THE term physiology is to include the study of function at all levels of organization from intact animals down to groupings of molecular components, a substantial fraction of the field does not seem to be generally and explicitly recognized as physiology in this country. This is true of microphysiology, and especially mammalian microphysiology. By microphysiology is meant the description of the functional properties of cells that are significant in whole animal physiology, as well as the explanation of these properties in terms of subcellular components down to molecular dimensions. A description of the rates and other characteristics of oxygen absorption by cells during rest and activity, supplemented by an explanation of such observations in terms of the cytochrome system, the tricarboxylic acid cycle, and the glycolytic system, provides an example of a segment of microphysiology dealing with a general property of cells. A description of the contraction of a single skeletal muscle fiber, its all-or-none response, the dependency of response on frequency of stimulation and initial length of fiber, together with the beginnings of an explanation of these properties in terms of actomyosin and ATP, is an example of a portion of microphysiology dealing with a property highly developed in particular cell types.

Microphysiology as here defined is an active research field in which physiologists are engaged, but, as large amounts of new information become available, the field is apparently not being comprehensively and systematically arranged as a part of physiology. This is revealed in the handling of the literature, the programming of our meetings, the content of textbooks, as well as in many aspects of our teaching. It should be feasible to base the arrangement of facts in this area on cellular physiological functions, rather than on organ system functions as in classical physiology, which fails to consider, or separates, some properties common to many cells. A few possible headings might be *Transformation and Transfer of Materials,* including a reorganized and unified approach to the subject matter covered in part under such topics as metabolism, nutrition, electrolyte balance, membrane properties, osmosis, absorption, secretion, excretion, energetics, control, and the steady state; *Maintenance and Functions of Structure in Living Cells; Adjustment to the Environment,* including general influences and response to specific stimuli; *Transfer of Excitation; Movement;* and *Growth*—in all cases associated with related facts of the underlying integrated system of enzymatically catalyzed reactions. Within limits this is done in general physiology, but only in those phases of the subject that can now be expressed in physical and chemical terms or that are largely descriptive of cellular activity without much reference to chemical components.

Microphysiology as thus outlined would emphasize those properties of cells through which they act as the functional units at organ-system and intact-animal levels of organization. Descriptive information of such properties is currently limited, except for some characteristics of a few cells like the skeletal muscle fiber. On the other hand, the need for *understanding* what is described at the cellular level of organization would also be underscored. Complete understanding cannot be gained either from a description of the highly organized system, the cell, or from analytical studies of the molecular and other components of the cell. The latter, which is biochemistry, must be combined with the former, a part of physiology, no matter how great the present gulf may be. To cite a comparable analogy, few would claim that circulation of the blood is not a part of physiology just because its understanding depends on pure physics.

The long-range goal of microphysiology, whether mammalian or general, is the integration of the cellular components having certain physical and chemical characteristics into a unified system or set of systems out of which the observed cellular functions will emerge.

RUBERT S. ANDERSON
School of Medicine, University of South Dakota

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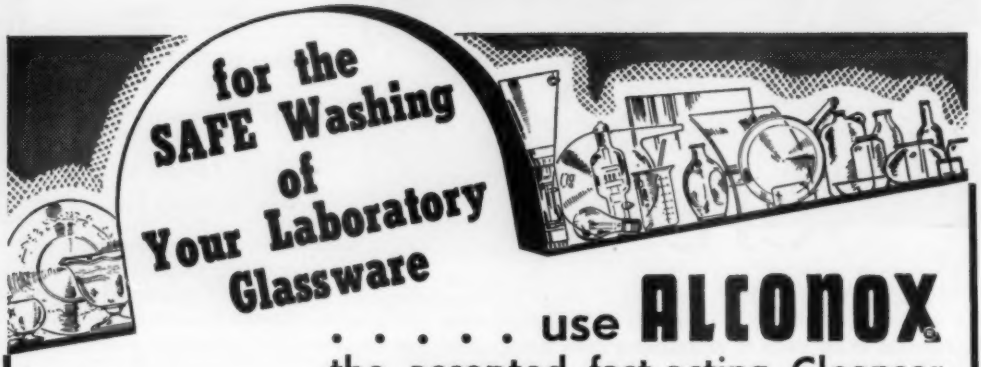

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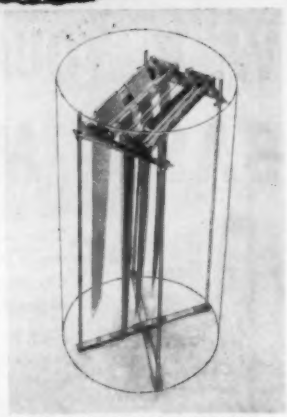

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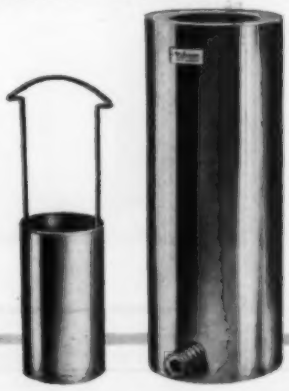

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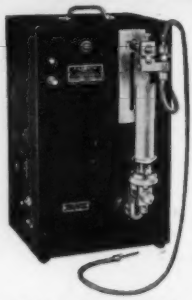

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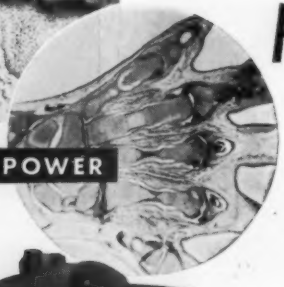

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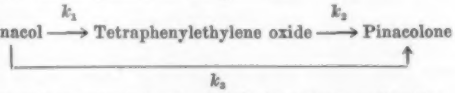
Washington University and St. Louis University, St. Louis, Missouri

Molecular Rearrangements of Aryl Pinacols and the Theory of Neighboring Group Displacement Reactions

Kenneth H. Adams and Herbert J. Gebhart, Jr.

St. Louis University

A kinetic study of the acid-catalyzed rearrangement of benzopinacol (tetraphenylethylene glycol) in acetic acid solution has shown that the pinacolone is formed by way of two simultaneous reactions. Approximately 80% of the pinacolone is formed by a reaction path that involves tetraphenylethylene oxide as an intermediate, whereas the remainder of the product is formed by a direct rearrangement of the pinacol:



The rate constants k_1, k_2, and k_3 have been evaluated.

From the point of view of neighboring group displacement theory, these results indicate that participation by C_β-hydroxyl is considerably greater than that by C_β-phenyl in this reaction. Whether this is due to a thermodynamically favored participation by C_β-hydroxyl or to the decreased participation of C_β-phenyl attributable to steric factors requires consideration. There is considerable evidence that the steric factor is important in these reactions.

Orthoquartzites in Missouri

Victor T. Allen and James T. Lift

St. Louis University

The LaMotte sandstone of Cambrian age, the Roubidoux, Everton, and St. Peter sandstones of Ordovician age, the Bushberg and Aux Vases sandstones of Mississippian age, and the Graydon sandstone of Pennsylvanian age in Missouri were studied petrographically.

According to Krynine's terminology, parts of these formations are orthoquartzites. The samples studied are of sedimentary origin, are composed of 95% or more quartz, and some have a silica cement. In much of these formations the silica cement is scanty or lacking and the sandstones are friable. Locally, the silica cement is absent, and carbonates, iron oxides, and clay are the cementing materials. The term "orthoquartzite" is unsatisfactory, because to some it indicates a well-indurated sandstone and to others a metamorphic rock. Long usage, as well as petrographic study, indicates that "quartzose sandstone" is a better term for these sedimentary rocks. Where desirable the nature of the cement can be indicated by the use of adjectives, such as silicinate and calcarinate; this was proposed in 1936 by the Subcommittee on Nomenclature of the Committee on Sedimentation of the National Research Council.

The Mathematical Development of the Formulas Essential to the Intelligent Use of Countercurrent Separations where the Number of Passes is Less than Twenty Five

Willard M. Allen

Washington University School of Medicine

Countercurrent distribution of several compounds between immiscible solvents has proved to be a very useful method of separating mixtures of both known and unknown compounds. These separations can be carried out either in a series of separatory funnels or in semiautomatic machines.

When the compounds in question have sufficiently different solubility constants, the number of distributions necessary to achieve virtually complete separation can be materially reduced by selecting the proper ratio of volumes of the upper and lower layers. Further, it is relatively easy to calculate the total amount of a given compound that is present in all the tubes from analysis of the amount present in either phase in tubes at or near the maximum.

The mathematical considerations necessary for the selection of the optimum ratio of the upper and lower layers, the calculation of the distribution constants, and the total amount of the compounds present are given.

The Ecology of Introgression in *Adenostoma*

Edgar Anderson, *Washington University*

Among variation patterns studied in various plant populations, one of the most curious was in *Adenostemma fasiculatum*, a component of the California chaparral, particularly in burned-over areas. It varied widely in inflorescence pattern from plant to plant, although it was frequently uniform in other characters. Analysis demonstrated that this variation was centered around (1) a low dense-flowered complex with short, wide leaves, and (2) a tall open-panicled complex with long, narrow leaves. The latter was found growing in the "Mother Lode" country. By extrapolation, a description of the other hypothetical parent was drawn up in such detail that it was identifiable as *Adenostemma fasiculatum* var. *obtusifolium*, native to islands and headlands in southern California. A re-examination of Adenostemma populations indicated them as varying widely between these two extremes, each of which contributes a character complex valuable in certain microhabitats of the chaparral but not in others. The low complex grows in thin soil under intense radiation but is not inured to long waterless periods. The tall complex can endure drought but has deep soil and less radiation. Each of these habitats (sea-coast and oak-savannah) is known to be geologically ancient, whereas the chaparral is comparatively recent. The combined evidence presents Adenostemma as a variable bicentered complex of hybrid origin, still highly plastic and

in a state of rapid evolutionary flux under the violent impact of man.

Recent Studies of Petrified Plants from the Central American Coal Fields

Henry N. Andrews, Jr., *Washington University*

During the past ten years petrified plants have been collected in some abundance from the Pennsylvanian age coal seams of the Central States, particularly Indiana, Illinois, Missouri, Iowa, and Kansas. These occur as calcified masses of plant remains, known as coal balls, which are found in the coal itself. At present they are known from numerous localities representing a wide stratigraphical range through the Pennsylvanian.

The fossils found in these petrifactions include several groups of early seed plants, as well as abundant ferns and fern relatives. Our study of them has been undertaken chiefly to shed further light on the evolution of these groups and to trace connections with the more recent derivatives.

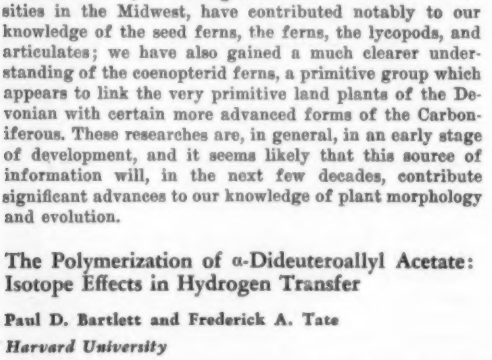
The study technique involves, first, rather extensive field exploration to obtain representative collections from as many different horizons as possible; these are prepared in the laboratory with the nitrocellulose peel method, the resultant sections being studied in essentially the same way that serial sections of a modern plant are dealt with.

These studies, now being carried on at several universities in the Midwest, have contributed notably to our knowledge of the seed ferns, the ferns, the lycopods, and articulates; we have also gained a much clearer understanding of the coenopterid ferns, a primitive group which appears to link the very primitive land plants of the Devonian with certain more advanced forms of the Carboniferous. These researches are, in general, in an early stage of development, and it seems likely that this source of information will, in the next few decades, contribute significant advances to our knowledge of plant morphology and evolution.

The Polymerization of α-Dideuteroallyl Acetate: Isotope Effects in Hydrogen Transfer

Paul D. Bartlett and Frederick A. Tate
Harvard University

It has been shown previously that in the polymerization of allyl acetate the chain-propagating and chain-terminating steps represent different modes of interaction between the same two molecular species:



Any change in the ratio $\frac{k_p}{k_t}$ between the rate constants for chain-propagation and chain-termination would be expected to affect both the average molecular weight of the polymer and the amount of polymer produced by a given amount of free-radical initiator.

Replacement of the α-hydrogen atoms of allyl acetate by deuterium indeed produces an increase of two- to threefold in these quantities. The results confirm the proposed mechanism of polymerization, since the termination reaction involves the transfer of hydrogen from one carbon atom to another and the propagation reaction does not.

There are indications in recent work that the magnitude of the isotope effect in hydrogen transfer reactions is a function of the electrical polarity assumed by the hydrogen during its transfer. These indications are discussed in terms of reaction rate theory.

Molecular Weight Determination by the Equilibrium Ultracentrifuge

J. W. Beams, A. Robeson, and N. Snidow
University of Virginia

Of the two general methods for determining molecular weights by the ultracentrifuge, the equilibrium method is the most reliable because it is based directly upon thermodynamic theory. The quantities measured in the equilibrium method during the centrifuging process are the rotor speed, the rotor temperature, and the concentration of the material under investigation across the centrifuge cell. In addition, the rotor speed and temperature must be held constant (or allowed to change slowly by a known amount) over a long period of time. The partial specific volume of the substance, which also must be known, is determined in separate experiments.

In the experiments here described the ultracentrifuge rotor is magnetically suspended in a vacuum and driven to the desired speed by an air turbine situated below the vacuum chamber. A thin, flexible shaft which passes through a vacuum gland connects the turbine and rotor. At operating speed the shaft is disconnected and the rotor coasts freely during the experiment, which usually extends over several days. The deceleration of the 7.5" diameter rotor is approximately 1 rps/day, and the rotor speed can be measured to one part in 10 million if so desired. The rotor temperature is held constant to within 0.01° C. The refractive index across the centrifuge cell, from which the concentration is found, is determined by a special interferometer method in which a fringe shift of less than 0.1 fringe can be measured. As a result, the precision is greater than in previous experiments and the observation can be extended to more dilute solutions.

The Limiting Thickness of an Electrolyzed Gas Film Capable of Sustaining a Given Negative Pressure

Lyman J. Briggs, *National Bureau of Standards*

The critical thickness of a gas film that is just capable of withstanding a given negative pressure P_N in a liquid column has been studied. The film was generated electrolytically on the surface of a spherical platinum electrode of known area. The number of gas molecules correspond-

ing to the measured charge required to release the negative column was then computed from the relation between the Faraday constant and Avogadro's number. The number of gas molecules required to form a monolayer on the electrode was next computed from the molecular diameter, based on van der Waals' equation. The ratio of these numbers gives the thickness, t, of the film in fractions of a monolayer.

Both H_2 and O_2 gas films were used. Measurements were made at various negative pressures, ranging from $P_H = 160$ cm water, $t = 0.54$ monolayer, to $P_H = 8.5$ cm, $t = 0.99$ monolayer. The results lie on a smooth curve, represented approximately by the equation $P_H = kt^{-5}$; i.e., the effectiveness of the film is inversely proportional to the fifth power of its thickness.

Throughout the range of these experiments, the film is less than one monolayer in thickness, becoming complete when $P_H = 10$ cm water. The computed thickness varies with the value chosen to represent the diameter of the molecule.

Color Markings on Pennsylvanian Pelecypods

Kenneth G. Brill, Jr., *St. Louis University*

Traces of color markings have been found on three genera of pelecypods from upper Pennsylvanian strata in San Miguel Co., N. M.

Streblochondria sp., a smooth-shelled pectinoid, shows about nine dark bands alternating with wider light bands. All bands radiate from the beak.

Acanthopecten carboniferous, a pectinoid, has dark concentric growth lines studded with dark spinous processes on a lighter background.

A form that is probably *Edmondia gibbosa* has a light surface speckled with dark. The minute spots are arranged in rows radiating from the beak.

The pelecypods occur with bryozoans, brachiopods, and gastropods in a yellowish-gray calcareous silty shale. None of the other fossils shows evidence of color markings.

Mechanism of Lysis of Bacteria by Bacteriophage

J. Bronfenbrenner, *Bowman-Gray Medical School*

The mechanism responsible for the lysis of the phage-infected bacteria has not received much attention; a review of existing evidence pertaining to this subject may therefore be of interest.

If a freshly seeded culture of bacteria is divided into two portions and a moderate amount of phage introduced into one of them, such phage-infected culture becomes turbid sooner than the control because of the accelerated growth of bacteria. After a relatively short period, however, this turbidity rapidly disappears as the result of lysis of bacteria. At this time the amino nitrogen content of the lysed culture is found to be considerably higher than that of the uninfected control. Microscopic examination reveals that during the period preceding lysis the infected bacteria undergo considerable swelling and, eventually, sudden disintegration, as if by bursting.

If one seeds bacteria upon the surface of a solid medium containing a relatively high concentration of agar or gelatine, bacteria still respond to infection with phage by exhibiting increased rate of multiplication, but the swelling and lysis are prevented. However, incorporation of appropriate concentrations of urea into such media permits the swelling and lysis of bacteria to take place.

These observations suggest that the primary result of exposure of susceptible bacteria to bacteriophage consists of markedly increased bacterial metabolism accompanied by hydrolysis of cytoplasm and the resulting increase in the intracellular osmotic pressure. If free water is available, it enters the bacterial cells, causing them to swell and eventually to burst. If one sets up competition for water by increasing the concentration of agar in the medium, the swelling and bursting of cells are prevented. Highly diffusible ions of urea, being highly hydrated, penetrate the cells and accomplish the transfer of water against competition by agar and thus make possible the swelling and bursting of bacteria.

Characteristics of Thunderstorm Microbarograms

Edward M. Brooks, *St. Louis University*

The following outline indicates the classification used:

I. Microcyclone
   - *a*) With tornado (tornado cyclone)
   - *b*) Without tornado

II. Pressure rise
   - *a*) Pressure jump
   - *b*) Before thunderstorm high

III. Thunderstorm high
   - *a*) Accentuated by hail
   - *b*) Well-developed thunderstorm
   - *c*) Shower or weak thunderstorm

IV. Pressure drop
   - *a*) Rear of well-developed thunderstorm
   - *b*) Rear of shower or of weak thunderstorm

V. Rear low
   - *a*) With strong convergence (sometimes producing arched cloud)
   - b) Behind shower or weak thunderstorm

The Effects of Pre- and Postnatal Anoxia upon Learning and Memory Ability at Maturity

Marion E. Bunch, *Washington University*

Approximately 450 white rats were used in investigating (1) the effects of severe oxygen deprivation (3% equivalent oxygen for 30 min) within 2 hr after birth upon the ability to learn and remember at maturity, and (2) the effects of severe oxygen deprivation during the fetal period upon learning ability at maturity. In the latter condition, pregnant females were exposed to simulated altitudes of 30,000′ for 2 hr. Of the offspring, 100 learned the maze problem as adults and were compared with 100 normals at same age. Littermate controls were used in the first part of the study.

The principal learning problem for the rats on which this report is based is the multiple-T 14-unit water maze. Standard procedures were used in measuring learning and retention; retention interval was 30 days. Animals were started on learning tasks at approximately 70 days of age.

Results: Ability of white rats at maturity to learn and remember a difficult maze problem is not affected by severe exposure to anoxia (3% equivalent oxygen) for 30 min within 2 hr after birth. The effects of severe exposure to anoxia during the fetal period upon learning ability at maturity were marked and statistically signifi-

cant. The anoxic animals were decidedly inferior to their controls in the measures of learning.

A New Case of Cryptic Species in *Drosophila*

Hampton L. Carson, ***Washington University***

A Brazilian species of fruit fly, *Drosophila bocainensis* Pavan and da Cunha 1947, has been shown by the examination of salivary gland chromosomes to consist of three discrete populations which do not interbreed under natural conditions. These entities may thus be properly described as species, despite the fact that there are only obscure and cryptic morphological and physiological differences between them. Two of these specific entities, *D. bocainensis* (*sensu stricto*) and *D. parabocainensis*, although they coexist in the same geographical areas without hybridization, freely interbreed under laboratory conditions, with luxuriant production of offspring. Tests of these hybrids have shown that, unlike previous cases in this genus, they are highly fertile, with the exception of one type of hybrid male that is only partially fertile. No information exists concerning the factors that effectively prevent crossing between these "sibling species" in nature, although there appear to be reciprocal changes in frequency of the two species with season, suggesting that ecological differences are involved. No hybrids have been obtained between the third entity, *D. bocainoides*, and either of the other two, and this species is clearly somewhat separated from them phylogenetically. These findings have important implications with regard to problems of the mechanics of isolation and evolution.

Immunologic Studies of Fetal Hemoglobin

Amoz I. Chernoff

Washington University School of Medicine

Techniques have been developed, using antifetal hemoglobin serum of high potency and specificity, for the qualitative and quantitative determination of fetal hemoglobin (F hemoglobin) in human blood specimens. The production of antihemoglobin sera of high titers has been made possible by the use of adjuvant mixtures to increase the antibody response evoked by the weakly antigenic material. In the present investigation, pure fetal hemoglobin has been employed as antigen. The latter was separated from other forms of human hemoglobin by taking advantage of the resistance of fetal hemoglobin to denaturation by highly alkaline reagents. Absorption studies suggest that the antifetal serum is specific for the embryonic pigment. A quantitative precipitin reaction, based upon a straight-line relationship between the logarithm of the time in minutes required for the precipitin ring to become apparent and the logarithm of the amount of F hemoglobin, has permitted the estimation of extremely small quantities of this compound.

Results of the study reveal that (1) fetal hemoglobin occurs in normal adult individuals in small amounts, the maximum being less than 1.0% of the total hemoglobin and, in general, less than 0.5%; (2) the alkali-resistant hemoglobin fractions detected by the denaturation technique in many instances of the hereditary hemolytic syndromes, and occasionally in acquired hematologic diseases, are immunologically identical with normal fetal hemoglobin. Comparative results between the values for F hemoglobin obtained by the alkali-denaturation technique and the quantitative precipitin test were in excellent agreement.

A Study of Oxidative Phosphorylation with Oxygen 18–Labeled Phosphate

M. Cohn, ***Washington University School of Medicine***

An attempt has been made to gain some insight into the nature of the interaction between oxidation from substrate through the electron transport system to oxygen and phosphorylation by labeling the inorganic phosphate which participates in these reactions with oxygen 18. The rationale of the method was based on the probability that the phosphate group does not proceed through a series of reactions intact but may lose one or more of its original oxygen atoms.

A new reaction which occurs in oxidative phosphorylation associated with the electron transport system has been observed in rat liver mitochondria with α-ketoglutarate, β-OH butyrate, and succinate as substrates. This reaction manifests itself by a replacement of oxygen 18 and parallels the phosphorylation associated with the oxidation. The number of molecules of inorganic phosphate which participate in this reaction, calculated on the basis that a monoester of phosphate is involved, is several times higher than the number of high energy phosphate bonds that can be formed. The reaction does not occur at the substrate level oxidation of α-ketoglutarate, and the evidence suggests that it occurs at every step in the electron transport system.

This phosphate turnover reaction occurs only when phosphorylation is proceeding. Dinitrophenol suppresses the reaction. The omission of Mg^{++} or adenylic acid also suppresses the reaction. The possibility that the reaction is due to a direct reaction of ATP, hydrolytic or otherwise, is eliminated. Various mechanisms which are consistent with the findings are discussed.

Studies on the Biosynthesis of Tobacco Mosaic Virus

Barry Commoner, ***Washington University***

The reduplication of tobacco mosaic virus in tobacco leaf has been studied by comparing nitrogen metabolism of infected and uninfected tissue. Changes in the following components during virus biosynthesis have been quantitatively determined: tobacco mosaic virus; total nitrogen; total protein; total nonprotein nitrogen; free ammonia, amide and amino nitrogen; individual free amino acids and amides. Changes in a series of protein fractions have also been studied by electrophoresis and by other means. The data show that: (1) Synthesis of virus induces withdrawal of host nonprotein nitrogen (chiefly ammonia, glutamine, asparagine, glutamic and aspartic acids, and serine). (2) Previous to virus formation, infected tissue synthesizes an excess (as compared to uninfected tissue) of an insoluble protein component. (3) During virus formation a transitory excess of soluble protein occurs. (4) Several specific soluble low molecular weight proteins are synthesized along with the virus in infected tissue.

These observations and investigations of infected tissue cultured in nutrient containing N^{15}-labeled ammonium ions lead to the following conclusions: (1) Virus protein nitrogen is derived from free ammonium nitrogen, with-

out passing through the pool of free amino acids and amides. Therefore, virus protein synthesis involves *de novo* formation of peptide bonds either from ammonia or from a component derived from ammonia which is *not* free amino acid or amide nitrogen. (2) The nonvirus soluble proteins synthesized *de novo* in infected tissue may represent virus precursors. (3) The site of synthesis of virus or of its protein precursors is probably an insoluble cell particulate.

Man's Awareness and the Limits of Physical Science

A. H. Compton, *Washington University*

Attention is called to the conflict between the views of Bohr and Schrödinger regarding the nature of the physical world. Bohr considers this to include only that which can in principle be verified by observations using material instruments. Schrödinger introduces the hypothesis of a physical continuum, typified by the concepts of wave mechanics, whose changes follow a strictly causal determinism, but of which observations with material instruments can give only partial information.

Making use of Bohr's evidence that one's awareness of his intentions makes possible the prediction of his actions more definitely than is in principle possible from physical observations, a category of ideological reality is introduced. This category includes feelings, ideas, intentions, etc., of which one is immediately aware. It is distinguished from the physically real world as defined by Bohr. In terms of this distinction, Schrödinger's determined continuum has ideological but not physical reality. The question remains whether this continuum may have objective reality outside the physical world.

The usefulness of one's awareness of his intentions in forecasting physical events suggests the following rather obvious hypothesis: that there exists an objective world regarding which physical observations reveal one aspect and man's awareness reveals another. Such a world is not evidently related to Schrödinger's continuum. The present hypothesis can, however, be used in reconciling the "outer" physical indeterminateness of man's actions with a high degree of "inner" determinateness. Here seems to be an answer to Schrödinger's criticism of the concept of an undetermined world as violating the reasonable inference of self-determined actions associated with the sense of moral responsibility.

Structure of Glycogen and Enzyme Patterns in Glycogen Storage Disease

Gerty T. Cori

Washington University School of Medicine

Understanding of the mechanisms of action of the 3 enzymes necessary for the synthesis and breakdown of glycogen has been helpful in the elucidation of the structure of glycogen. These enzymes are: (1) phosphorylase, which catalyzes the synthesis and breakdown of the prevalent 1 : 4 maltosidic linkage; (2) amylo-1,6-glucosidase, which catalyzes the hydrolytic fission at the branch points, with glucose as one of the reaction products, and which acts only after exhaustive phosphorylase action; (3) the "branching enzyme" (a transglucosidase) which exchanges an α 1 : 4 for an α 1 : 6 link, transferring a chain of about 3 glucose residues, probably within the same branch.

Studies with these enzymes have led to a formulation of glycogen as being a treelike compound, confirming the postulations, based mainly on physical measurements, of K. H. Meyer.

Enzymatic structure analyses were carried out on animal and plant glycogens. The percentage end group varied from 8.3 to 5.8, showing that there exists a continuous series, and not just the two extremes, as had been claimed previously. In most cases of glycogen storage disease, no deviation from the normal pattern was found. There were, however, two exceptions: one case in which muscle and liver glycogen had a branch point percentage of 13 and 11, respectively. This was due to the outer chains being extremely short so that the 2 polysaccharides resembled phosphorylase limit dextrins. In the second case, only liver glycogen was available for analysis. It resembled closely the branched fraction of starch (amylopectin) in having a branch point percentage of only 4.7. It also had the physical characteristics of amylopectin (iodine color, solubility, x-ray diffraction pattern). In a number of cases with normal glycogen structure, autopsy and biopsy specimens of the liver were tested for glucose-6-phosphatase activity. In two fatal cases the enzyme was found to be at very low level of activity. In two out of four surviving storage disease cases, all with mild symptoms, the activity of the glucose-6-phosphatase was below the level found in other liver diseases. The pathogenesis of the disease in terms of deficiencies of several enzymes is discussed.

A Possible Mechanism of Excitation of Nerve Impulses in the Cochlea

Hallowell Davis and Ichiji Tasaki

Central Institute for the Deaf

In the cochlea the membranous labyrinth, filled with endolymph and containing the sensory cells for hearing (in the organ of Corti), lies on the basilar membrane and forms part of the so-called cochlear partition between the scala vestibuli and the scala tympani. It constitutes the "scala media." Mechanical movements of the cochlear partition somehow initiate nerve impulses in the nerve fibers that innervate the sensory cells. We suggest that the sensory cells do not themselves respond like nerve fibers but serve to modulate a flow of electricity from the scala media to the scala tympani.

Some important facts on which this hypothesis is based are: (1) There is a large d-c electric potential across the organ of Corti and basilar membrane between scala media and scala tympani. (2) An alternating electric potential closely related to mechanical vibration of the cochlear partition seems to originate at the specialized ends of the sensory cells—i.e., at the surface in contact with the endolymph in scala media. (3) The two potentials are closely related to one another and depend on an adequate oxygen supply. (4) The alternating potential and nerve impulses are more sensitive to changes in potassium concentration in scala tympani than in scala vestibuli. It is therefore likely that the specialized ends of the sensory cells and not the basilar membrane are the major barrier to electric current flow from scala media to scala tympani.

Two major assumptions are: (1) Mechanical move-

ment of the specialized "hairs" of the sensory cells in the proper direction alters the resistance of the major electrical barrier. (2) The energy that maintains the positive potential of scala media is derived from the metabolism of the stria vascularis, a glandlike structure in the scala media close to its blood supply.

According to this hypothesis, the sense organ does not merely transduce the energy of the stimulus. The stimulus controls the release of additional energy from an especially available source. The organ is comparable to a carbon microphone circuit in which a change of resistance in the microphone modulates the flow of d-c current from a battery through a well-defined circuit. In the cochlea the nerve endings on the sensory cells are part of this circuit and can be stimulated by the changes in the current flowing through them.

Several features of the anatomy of the organ of Corti, the stria vascularis, etc., that lend support to this hypothesis are pointed out.

The Chemical Characterization and Submicroscopic Structure of Elastic Tissue

Edward W. Dempsey

Washington University School of Medicine

Elastic tissue occurs variously in mammals as fibers ranging from 5 μ in diameter to the limit of microscopic visibility, and as fenestrated lamellae. In different species, locations, and ages, elastic tissue exhibits minor differences in staining reactions, but in general it is characterized by an extremely slight affinity for acid or basic dyes and by a selective affinity for orcein when applied in acid alcoholic solutions. These latter dyes contain phenolic groups, and their uptake can be prevented by previous saturation of the elastic tissue with naphthoic compounds. Irreversible or competitive reaction of the acid or basic radicals does not alter the affinity of elastic tissue for orcein. The uptake of orcein is influenced only slightly by pH. Such results indicate that the bond uniting orcein and elastic tissue is not ionic, but some other type of interaction.

Elastic fibers are insoluble in all ordinary solvents. An enzyme, elastase, renders the fibers soluble without forming free amino acids. During digestion large fibers split longitudinally into two smaller fibers; these in turn cleave into still smaller fibers. Observations made with the electron microscope indicate that small fibrils (*ca* 200 A in diam) are ultimately produced. Thin sections of elastic fibers and plates, shadowed with chromium, reveal that these small fibers are arranged in an anastomosing network, randomly oriented in the relaxed fiber. In stretched fibers, these fibrils become increasingly parallel, thus forming a basis for the fact that elastic tissue is isotropic when relaxed but birefringent when stretched.

A Comparison of the Metabolism of some Female Sex Hormones

E. A. Doisy, Jr., B. C. Bocklage, N. H. Shen, and A. F. Valcourt

St. Louis University School of Medicine

In these studies progesterone-21-C^{14}, 17-C^{14} H_3-estradiol-17β, synthesized in our laboratories, and commercially available estrone-16-C^{14} were administered separately to three main types of adult spayed rats of the St. Louis University colony. Doses within the physiological range were employed whenever possible. The excreta and, in some instances, expired CO_2, bile, and lymph were collected for C^{14} assay.

No significant amounts of $C^{14}O_2$ were present in the expired air of animals receiving 17-CH_3-estradiol, but animals receiving progesterone excreted up to 15% of C^{14} in the expired air. Normal animals excreted the majority of the administered C^{14} in their feces, whereas values from 56 to 96% of the administered C^{14} were found in the bile of rats with bile fistulas. It is apparent that the liver of the normal animal constitutes the major excretory pathway of C^{14} in these compounds.

Animals in which the bile ducts had been doubly ligated and severed excreted most of the C^{14} in the urine, showing that the kidney can assume this role of the liver when the flow of bile has been interrupted. In addition, acute experiments on the routes of absorption and distribution in tissues have been performed.

The Metabolism of Androgens

William H. Elliott, James Ashmore, and Paul M. Hyde

St. Louis University School of Medicine

Representative androgenic steroids labeled with C^{14} have been prepared and utilized in a study of the metabolism of the male sex hormones in the rat. In experiments carried out over a period of 4 days following intramuscular or intragastric administration of physiological quantities of testosterone-4-C^{14}, 17-methyl-C^{14}-Δ^5-androstene-3β, 17β-diol, or 17-methyl-C^{14}-testosterone, most of the radioactive metabolites were found in the feces of normal animals and in the bile of animals with bile fistulas. When the biliary role of excretion was blocked by ligation of the bile duct, the kidney assumed greater importance as an excretory organ, since the major amount of radioactivity was always found in the urine in these experiments.

Studies on the hydrolysis of the biliary radioactive metabolites of testosterone have demonstrated the presence of a major portion in the form of glucuronides.

Steroid Compounds Resulting from Incubation of Cortisone with Surviving Liver Slices

Albert B. Eisenstein

Washington University School of Medicine

The ability of surviving liver tissue to alter the chemical structure of steroid hormones has been demonstrated. These studies have been concerned primarily with inactivation of androgenic and estrogenic substances. Adrenal steroids have not been extensively studied in this manner, although Schneider has recently reported catabolism of cortisone by rapid reduction of the conjugated unsaturated bonds in ring A of the molecule and extensive degradation of the α-ketol side chain when incubated with rat liver slices.

The purpose of the present study was to determine if cortisone is actively metabolized by surviving liver slices and to detect and characterize any new compounds that might result from such metabolic processes.

Rat liver slices were incubated in the presence of small amounts of cortisone. After incubation the steroid frac-

tion was recovered and analyzed by paper chromatography. Chromatograms demonstrated the presence of 3 steroid compounds.

The steroids were eluted and then characterized by determination of absorption spectra in ultraviolet light, by formation of sulfuric acid chromogens, by certain color reactions, and by comparison of mobility on paper with that of known compounds.

The compound that moved most rapidly on paper was cortisone, unchanged by incubation. The second compound, of intermediate polarity, proved to be Compound F. The third, and most polar steroid, is not completely identified. Analysis indicates that this substance retains the conjugated unsaturated bonds but the α-ketol side chain at C-17 is altered.

The results demonstrate that the liver can convert cortisone to Compound F. Since Compound F is biologically active, this evidence indicates that the liver metabolizes steroids not only by inactivation but may produce other active hormonal substances.

Fructose as a Source of Calories during Intravenous Alimentation

Robert Elman and Theodore E. Weichselbaum

Washington University School of Medicine

Starvation was formerly inevitable and sometimes fatal in patients unable to eat. Injection of needed nutriments directly into the blood stream (intravenous alimentation) in such cases has already extended greatly the boundaries for the conquest of disease. To supply calories in this way the carbohydrate glucose (dextrose) has been employed. Glucose has the disadvantage of remaining outside the cell for some time after infusion, which leads to a large loss of sugar in the urine. Fructose, a carbohydrate widely distributed in nature, and just as effective as glucose as a source of calories, was found to enter the cell rapidly and to appear in only small amounts in the urine. More important, fructose is better than glucose for protein synthesis from infused amino acids, which are often given as part of the intravenous diet as a source of protein food. The reason is that after intravenous infusion amino acids enter the cell just as rapidly as fructose, both being metabolized together, the one for energy, the other for protein synthesis. By contrast, amino acids given with glucose tend to be used for calories rather than protein synthesis, because energy needs are given first priority and the infused glucose at this time is still outside the cell. The thesis that fructose is a better source for calories than glucose during intravenous feeding is supported by evidence obtained from observations made in human subjects.

The Lipotropic Action of Proteins

C. A. Elvehjem, *University of Wisconsin*

Twenty years ago Best and co-workers demonstrated that rats fed diets low in protein developed fatty livers and that choline added to the ration prevented the accumulation of this fat. Later it was shown that the accumulation of fat decreased as the level of protein in the diet was increased. Tucker and Eckstein showed that this lipotropic action was related to the methionine present in the protein. During our studies on the relation of tryptophan to niacin metabolism, diets containing 9% casein were used; we were surprised to find that the level of liver fat was above normal even when adequate amounts of choline or methionine were supplied. When choline was omitted from the basal ration containing 9% casein, the liver fat was 20–25% on the fresh weight basis. The addition of choline reduced the level to 8–10%, but a normal level of 3–4% was obtained only upon addition of 3–6% casein or gelatin. Individual amino acids such as proline, threonine, arginine, and glycine have some effect in reducing the amount of fat, but it appears that a combination of two or more amino acids is needed for the complete effect. These amino acids have no effect in the absence of methionine but function in addition to methionine in preventing the deposition of fat. When the carbohydrate in the ration is changed from sucrose to starch there is an increased rate of growth and a decrease in the liver fat, although a normal level is not reached. The possible relationship to the disease known as kwashiorkor is discussed.

Oil Structures Deduced from Soil Studies

Albert J. Frank, *St. Louis University*

A study of the heavy and light minerals and clay minerals of soils derived from Pennsylvanian rocks with known mineral content has made possible the drawing of structural maps in Illinois. The maps become inaccurate with increasing thickness of the Pennsylvanian section resulting from unconformities within the Pennsylvanian. Likewise, unconformities in the underlying rocks limit the method to near-surface rocks. With experience the soils can be identified at sight and possible structures seen from the air.

The Brodeur Biplane Serialograph

Lloyd L. Garner, *St. Louis University*

A report on the biplane serialograph, its various uses in research concerning heart and circulatory disorders, the branches of science used in its design and fabrication, and the special problems therein involved, is presented.

In the field of radiology, the biplane serialograph represents one of the greatest strides forward in the past decade and is the best method, to date, of obtaining serialized x-ray photographs for diagnostic purposes.

Cigarette Smoking and Cancer of the Lung

Evarts A. Graham, Ernest L. Wynder, and Adele B. Croninger

Washington University School of Medicine, Memorial Center, New York, and Washington University

Primary cancer of the lung has increased in frequency so much in the past 40 years that it is now the most common internal cancer in the male sex. Statistical studies, published by the authors in 1950, and a little later in England by Doll and Hill, are in remarkable agreement, showing that in cases of cancer of the lung there is almost always a history of excessive cigarette smoking for a period of at least 20 years and that it is rare to find a case in a nonsmoker. Also, we have obtained direct evidence that tar obtained from cigarette smoke will produce cancer experimentally when painted on the skin of mice

over a period of about a year. Demonstrations of the experimentally produced cancers are presented.

Factors Affecting the Viability of Influenza Virus Suspensions Subjected to the Freeze-drying Process

Donald Greiff, Herman Blumenthal, Masahiro Chiga, and Henry Pinkerton

St. Louis University

Using an all-glass, high-vacuum molecular still, PR8 influenza virus in allantoic fluid was lyophilized under different conditions. The apparatus permits the manipulation of any of 8 sets of duplicate ampules without disturbing the others. The end point of dehydration wns determined by using ionization gauges. At 10° C, for example, no further loss of water occurred after 3 hr. The factors studied were (1) the treatment of the material prior to dehydration, (2) temperature at which dehydration was carried out, and (3) the effect of incubation at 37.5° C on the dehydrated material. Dehydration at 26° C subsequent to precooling for 10 min at −80° C resulted in a higher rate of virus survival than did precooling at −30° C or 0° C. The titer of virus suspension precooled at −80° C was higher after dehydration at 0° C than after dehydration at −30° C, or under conditions such that the temperature rose from −80° C to −10° C over a 48-hr period. Virus lyophilized under various conditions showed no appreciable loss of titer on storage at −40° C; at 37.5° C, however, there was invariably some loss of titer, most marked during the first 3 days. This loss of titer on incubation was greater in virus suspensions dyhydrated at 0° C (which showed no loss of titer immediately after drying) than in suspensions lyophilized between −80° C and −10° C (which showed considerable initial loss).

An Investigation of the Concept of Integration

Stanley C. Grzeda, *St. Louis University*

The term "integration," current in psychological literature, is vague. It may denote an organizing process, an organized state, a reducing process, or be used as a synonym for adjustment. The present study was carried out to determine if a core of agreement exists among psychologists in their use of the concept of integration when rating combinations of responses to inventory questions.

The rating group numbered 49 and included both graduate students and faculty at the University of Illinois. Eighty-one pairs of questions taken from a personality inventory compiled by McQuitty were included in 4 rating scales. The materials were presented for rating following the procedure outlined below.

Each inventory question solicited one of three responses, *Yes*, *Between*, and *No*. For each pair of questions there were 9 possible combinations of responses: *Yes* to the first question and a *Yes* to the second, *Yes* to the first and a *Between* to the second, Y1–N2, B1–Y2, B1–B2, B1–N2, N1–Y2, N1–B2, N1–N2. Each of these combinations was rated according to the degree of integration reflected in it, in the judgment of the 49 psychologists.

Indexes of agreement were computed. The ratings for the question-response combinations were intercorrelated and factor-analyzed, using Thurstone's centroid method.

Results were as follows: (1) The indexes of agreement —i.e., average correlations—ranged from .07 to .90; the median was .51. (2) Two factors were abstracted, but one was thought to rise from conditions other than the question content. It is suggested that corrections in the wording of questions would have resulted in a single factor. (3) The items with the highest average correlations are related to McQuitty's integration measures.

The Role of Descartes in the Rise of Physiology

Thomas S. Hall, *Washington University*

The occasion of this report is the completion of the first English translation, as far as the author can discover, of Descartes' physiological essay, *Concerning Man*. In this paper, Descartes presents a thoroughly materialistic account of a variety of physiological functions and displays shrewd insights into physiological problems and issues of the mid-seventeenth century. His approach is that of asking the reader to imagine a marvelous machine capable of all the functions of which the human body itself is capable. Wherever possible, in describing the functions of the machine, Descartes draws on well-attested empirical fact. Where such fact is unavailable, he draws upon the speculations of earlier scientific thinkers and sometimes upon his own active imagination. This contradictory compounding of science and speculation is rendered more acceptable than it might otherwise be through the technique of using a hypothetical machine as the subject rather than man's body itself. Actually, the ruse is a thin one, and the admixture of fact and fancy becomes irritating to the serious reader at certain points. Scientifically, the essay is significant in being the first frank attempt to bring the totality of organic functions within the purview of Galilean mechanistic materialism. It gives the first well-elaborated and substantially correct account of physiological optics. Philosophically, it is significant in having established the famous Cartesian dualism, under attack in present-day systems, of matter vs. mind. Perhaps its chief effect lies in what it did to man's view of man, since it dared him to consider himself as something to be understood in terms of natural rather than transcendental philosophy.

Effects of a Diffusible Mouse Tumor Agent on the Growth of the Nervous System in the Chick Embryo

V. Hamburger and R. Levi-Montalcini

Washington University

The implantation of mouse sarcoma 180 and 37 into early chick embryos results in a selective growth promotion of spinal and sympathetic ganglia, whereas the somatic motor system is refractory. The tumor implants are invaded by large masses of fibers emerging from the hyperplastic ganglia. The growth-promoting agent is diffusible, as was demonstrated by the implantation of tumors onto the extra-embryonic membranes. In this case, not only was a striking overgrowth of the normal sympathetic ganglia observed but also a neoformation of atypical ganglionic masses. Large fiber bundles from these ganglia invade the adjacent viscera (mesonephros, gonads, spleen, thyroid gland, and others) which receive normally only a sparse innervation or none at all, at corresponding

developmental stages. The fibers do not establish synaptic connections.

The following points deserve further analysis: the chemical nature of the growth-promoting tumor agent and its selective effects; the apparent breakdown of the regulative mechanisms which normally prevent a hyperneurotization of viscera; the apparently unchecked spinning out of fibers; the question of whether the potential sympathoblasts or the viscera are the immediate target of the tumor agent; in the latter instance, the viscera would be induced to admit excessive numbers of nerve fibers and the latter would mediate the effect to the ganglia.

The Reliability of Measurements of Energy Metabolism

Francis L. Harmon, *St. Louis University*

Because of the widespread use of metabolism tests, both in clinical practice and research, the question of the reliability of such measurements is of crucial importance. Studies dealing with various aspects of this question have been reported; yet it remains a fact that the reliability of the metabolism test has not been satisfactorily determined to date. This seems to have been due partly to the application of relatively inefficient and, in some cases, inappropriate statistical methods to the problem, and partly to a faulty analysis of the problem itself. More specifically, previous investigators have not usually distinguished clearly enough between the stability of the metabolic rate and the precision with which the typical test measures this rate.

The general aim of the present study is to investigate the reliability of measurements made by the closed-circuit method upon 29 ostensibly normal, young adult males. Three steps are involved: (1) carrying out a complex analysis of variance upon a set of 348 test records, in order to isolate certain major sources of variation and evaluate the significance of each; (2) derivation, from the preceding analysis of a valid estimate of the error of measurement of the metabolism test; and (3) the establishment of other critical values for estimating the significance of changes in metabolic rate under certain specified conditions. Results obtained by this approach are described, together with examples of their applications.

Cutaneous Autonomic Reaction Patterns Servicing Temperature Regulation

A. B. Hertzman, W. C. Randall, and C. N. Peiss

St. Louis University School of Medicine

Cutaneous blood flow and sweating at various environmental temperatures exhibit definite regional patterns. Cutaneous vasodilatation is first observed on the fingers, then the toes and subsequently on other skin areas. Sweating begins on the dorsum of the foot, ascends the leg, appears on the hand, then the trunk and head. This order of recruitment suggests thermoregulatory spinal reflexes. After recruitment is completed, subsequent increases in cutaneous blood flow and sweating occur simultaneously over the entire skin surface, suggesting control by the hypothalamic centers. Considerable variation is exhibited in these patterns in various individuals. The extent of cutaneous arterial dilatation is less in some subjects than in others and implies corresponding differences in the circulatory loads imposed by heat.

Phenomena in the Liquid-Liquid Critical Region

Joel H. Hildebrand, George Jura, Don W. Fraga, and Gilda Maki

University of California

The critical point of a liquid-liquid system is customarily defined either by zero values of the first and second derivatives of activity with respect to total composition or by disappearance of the liquid-liquid interface. Additional criteria are available. The rapid increase in randomness of distribution, as a 2-phase mixture is raised to the critical region, suggested a corresponding increase in entropy. We have measured the heat capacity of a critical mixture of 2,2,4-trimethyl pentane and n-perfluoroheptane, from which association effects are absent, and found a steep cusp in the curve of heat capacity vs. temperature. Two liquids that are incompletely miscible dissolve in each other with large volume expansion, hence the volume-temperature curve also has a characteristic form with a break at the point of coalescence.

Certain Temporal Factors in Audition

Ira J. Hirsh

Central Institute for the Deaf* and *Washington University

This theoretical presentation attempts to show that the four basic physical dimensions, three of space and one of time, are not all equally important nor in the same order of importance for perception in all sense modalities. Theoretical and experimental literature on visual perception reveals a consistent preoccupation with spatial dimensions (primarily the two of the frontal plane), with relatively little concern for visual changes in time except for the studies on perceived movement.

Everyday visual perception is characterized by the discrimination of various shapes, extents, textures, and other qualities that are spread out in space. The referent for visual perception is the *object*. The important dimensions, therefore, are the properties of objects. Auditory perception, on the other hand, can rarely be referred to objects. We do not hear objects, but rather *events*. And the important dimension, therefore, for audition is the basic dimension for events—namely, time.

Study of the perception of time has been concerned mostly with comparison or absolute judgments of duration. It is proposed that time be used as a dimension in which stimuli are arranged or patterned in order to provide data that can describe the principles of operation of time-based sense modalities, such as audition.

If the above notions are correct, *visual acuity*, a measure of an *interval of space* between two visual stimuli that are perceived as two, is the important measure for predicting visual capacity for reading and other forms of discrimination of spatial patterns. The implication of these notions for audition is that the basic measure of auditory capacity is another *interval, now of time*, that is necessary in order that two successive acoustic stimuli are perceived as two. Lack of such a measure of auditory capacity, which is analogous to visual acuity, is largely responsible for the lack of good correlation between ex-

tant psychophysical measures of audition and the ability to perceive and discriminate adequately everyday auditory phenomena.

Exploratory experiments on temporal acuity or resolution in vision, audition, and tactual vibration reveal that these three senses differ widely with respect to the perception of temporal patterns. These, together with comparative results on auditory and visual fusion, reveal the clear superiority of audition when rapid stimulus changes are to be discriminated.

Photosynthesis: Old Problems in New Guises

Martin D. Kamen

Washington University School of Medicine

In recent years certain previously inaccessible areas of photosynthetic inquiry have been opened to biochemical research. This is owing, on the one hand, to the availability of isotopic-labeling methods combined with new analytic techniques that enable researches to be performed elucidating the character of intermediary metabolites formed during reaction periods of as little as a few seconds. On the other hand, noteworthy success in producing stable, active cell-free systems exhibiting a number of the partial reactions of photosynthesis has been achieved, whereby it has become possible to demonstrate that the photoactivation process produces reducing systems that may be coupled with any of a large variety of redox systems, including many that have been shown to be important in respiration. In addition, studies in bacterial photosynthesis have revealed some details of the manner in which synthesis of cell constituents is affected by photoactivation processes. The observations involved are discussed, and their interpretations in terms of current concepts of the photosynthetic process are considered. It is noted that the central problem of photosynthesis—i.e., the nature of the biochemical mechanisms that intervene between the initial photochemical act and the appearance shortly thereafter of certain photosynthetic products—may be reformulated and rephrased in many ways, but that as yet a direct approach to the elucidation of this problem remains to be found.

The Production of Bacterial β-Glucuronidase and its Use for the Hydrolysis of Steroid Glucuronides

Philip A. Katzman, Ralph A. Kinsella, Jr., and Miles L. Doyle

St. Louis University School of Medicine

Our interest in producing potent preparations of β-glucuronidase was prompted by the recognition of the need for mild yet effective methods for hydrolyzing the steroid conjugates that occur in urine, in other excreta, and in secretions.

Large amounts of β-glucuronidase are produced by *Escherichia coli* in the presence of menthyl glucuronide. Conditions for optimal production and activity of this enzyme have been determined, and some studies of its chemical and physical properties have been made.

The amount of total estrogen liberated from human pregnancy urine by this enzyme is as great as or greater than that obtained with acid hydrolysis. This indicates that the estrogen is conjugated to a very large extent with glucuronic acid.

Hydrolysis studies of the conjugated neutral 17-ketosteroids of the urine of normal men have shown that the major portion of this fraction is conjugated with glucuronic acid. This was not true in cases of adrenal tumors. It is believed that the distribution of the types of conjugates, as well as the total amounts of steroids, may be very important.

Since urinary corticosteroids are very labile to acid and heat, and since only a small fraction occurs in the free form, β-glucuronidase hydrolysis is important not only because it permits more accurate estimation of corticosteroid excretion but also because it gives better insight into the relative importance of urinary metabolites.

Incorporation of C^{14} Amino Acids into Peptides by Normal and Diabetic Rat Tissues

M. E. Krahl

Washington University School of Medicine

In severe diabetes there is loss of tissue protein with negative nitrogen balance; insulin, on the contrary, favors uptake of amino acids by tissues. The present experiments were undertaken to determine how insulin influences peptide synthesis.

Rat liver slices or diaphragms were incubated in a physiological medium containing glycine-1-C^{14} or phenylalanine-3-C^{14}; the radioactivity incorporated into the peptide glutathione and into the total proteins of the tissues was measured.

Incorporation of glycine-1-C^{14} into glutathione of liver was greatly reduced in severe diabetes, as was the uptake of both amino acids into the protein fractions of liver and diaphragm. This depression of glycine-1-C^{14} uptake into glutathione remained relatively the same when the glycine concentration in the incubation medium was increased by a factor of forty. From this it is concluded that the net decrease in glycine-1-C^{14} incorporation in diabetes is attributable in large part to decreased peptide synthesis; a limited concurrent increase in protein breakdown in diabetes is not excluded.

Glutathione synthesis by diabetic liver was raised toward the normal level by addition of glucose to the incubation medium, and completely to normal by addition of both glucose and insulin; without adequate glucose in the medium, insulin alone had no effect on amino acid uptake by diabetic liver. The conclusion is that the influence of insulin on peptide synthesis in liver is exerted mainly via its favorable effect on glucose utilization. Whether insulin increases peptide synthesis by any other mechanism remains to be determined.

The Dynamics of Total Systems in Psychology and Biology

George L. Kreezer, *Washington University*

The rapid rate of progress in the physical sciences and engineering has often been attributed to the effective use of mathematical methods. The possibility of using similar methods for theoretical treatment of the response systems of living organisms is not so generally acknowledged. Among the outstanding obstacles are the extreme complexity of biological systems and the lack of sufficient

information to permit writing the differential equations of a given system without extensive assumptions. The present paper outlines an approach that attempts to bypass these difficulties through the application of concepts derived from the engineering treatment of linear systems. Specifically, it attempts to derive mathematical functions to represent response systems from experimentally determined curves of the temporal response of the total system to specified forcing functions. It can thus be designated as an investigation of the dynamics of total biological systems, through a generalization of the meaning of dynamics in physics.

This approach is being carried out in two stages: (1) the development of methods for deriving system functions (transfer functions) from the response curves of biological systems, on the assumption that these systems are linear, and (2) the determination of signs of nonlinearity, from response curves, and the development of methods for taking account of them in the derivation of system functions. Illustrative records are presented of transient response curves of some psychological and biological systems, computer methods for deriving transfer functions, and some of the different types of nonlinearity observed. A graphical method for dealing with nonlinearity is briefly described.

A Differential Property of Plane Curves

P. Lanzano, *St. Louis University*

Given n plane differential elements of the second order E_i^2 $(i=1, \ldots, n)$ having distinct collinear centers, the dimension of the system of plane algebraic curves of order n (C^n) containing them will be

$$\nu = \frac{n(n+3)}{2} - (3n-\varepsilon) = \frac{n(n-3)}{2} + \varepsilon$$

$3n-\varepsilon$, $(\varepsilon \geqq 0)$, being the number of independent conditions imposed by the elements. As above system coincides with the one consisting of one curve (Γ^n) containing the elements together with $J^n \equiv \psi 3 \cdot C^{n-3}$ (ψ, line of the centers, C^{n-3} being arbitrary) whose dimension is $\nu = \frac{n(n-3)}{2} + 1$, so $\varepsilon = 1$; consequently, there must exist relationship among the coefficients of an analytic representation of the elements, which happens to be also sufficient for the existence of ∞^ν curves containing those elements.

Take $\psi \equiv y = 0$; any C^n having at the centers P_i $(\alpha_i; 0)$ the tangents $\tau_i \equiv \alpha_i - x + \beta_i y = 0$, will be (1) $\prod_1^n{}_i \tau_i = y^2$. C^{n-2} with arbitrary $C^{n-2} \equiv \sum_0^{n-2}{}_j \; a_j x^j + y \sum_0^{n-3}{}_j b_j x^j + \ldots\ldots + h y^{n-2}$.

If (1) must contain the

$$(i=1, \ldots\ldots, n),\ E_i^2\text{'s} \begin{cases} x = \alpha_i + \eta \\ y = p_i \eta + q_i \eta^2 + \ldots\ldots \end{cases}$$

it must be:

$$\frac{q_i}{p_i^3} \cdot \prod_1^n{}_k (\alpha_k - \alpha_i)_{(k \neq i)} = \sum_0^{n-2}{}_j a_j \alpha_i{}^j, \quad (i=1, \ldots\ldots, n)$$

the consistency condition of this linear system in the a's can be written (2)

$$\sum_1^n{}_i \left(\frac{q_i}{p_i^3}\right) = 0,$$

which, in a Euclidean metric, becomes

$$\sum_1^n{}_i \left(\frac{K_i}{\sin^3 \varphi_i}\right) = 0,$$

K_i's being the curvatures of the elements and φ_i's the angles between $\tau_i = 0$ and $y = 0$. (2) is the sought relationship.

Radioactive Isotope Separation by Nuclear Recoil

W. F. Libby and F. Sherwood Rowland

University of Chicago* and *Princeton University

As observed earlier, the two radiobromine isotopes formed by neutron irradiation of the two stable isotopes of ordinary bromine suffer sufficiently different excitation so that the Szilard-Chalmers hot atom reactions are perceptibly different. For example, the irradiation of alkyl bromides followed by aqueous extraction shows that the 4.5-hr Br^{80} is more completely extractable than the 35-hr Br^{82}. The phenomenon of the hot atom radioisotope separation of bromine has been investigated in more detail, and has been found to occur only in the solid phase. No observable effect has been found in the liquid, even though the liquid be at the melting point of the solid. The effect of molecular structure has been investigated in a limited fashion and found to be very considerable.

These observations are discussed in the light of a possible explanation in terms of the Br^{80} possessing a higher recoil energy than the Br^{82}.

The Structure of Nucleic Acids: A New Method of Degradation

David Lipkin and Jonathan S. Dixon

Washington University

Various physical and chemical methods have been used in order to gain information concerning the structure of nucleic acid macromolecules. The chemical methods that have been applied are (1) acid-base titrations of various groups in nucleic acid molecules; (2) hydrolysis catalyzed by acid, base, or enzymes; and (3) "blocking" of active groups in the nucleic acid, followed by degradation to small, identifiable fragments.

A new degradative procedure being developed is the base-catalyzed methanolysis of nucleic acids. An advantage of this approach over hydrolysis is that one part of any bond which is broken in the reaction becomes labeled with a methyl group. Thus, if a phosphoric acid group is attacked which is esterified to only two nucleosides, a methyl ester of a nucleotide or a dimethylphosphoric acid should be formed.

The methanolysis is carried out under strictly anhydrous conditions, using methoxide ion as catalyst and methanol-formamide mixtures as solvent. Yeast ribonucleic acid, with one normal methoxide ion as catalyst, is completely methanolyzed in 1 hr at 65° C. After the reaction is complete, the resulting mixture is chromatographed on ion exchange columns. The chromatogram obtained contains about 14 peaks, in contrast to the chromatogram obtained on the same nucleic acid sample degraded by hydroxide-catalyzed hydrolysis.

The individual components of the chromatogram are analyzed for phosphorus, methoxyl groups, heterocyclic base, and vicinal glycol groups. An examination of the analytical data on the various fractions enables one to make deductions concerning the structure of the original nucleic acid molecule. The results obtained to date are discussed.

Organismal Differentials and Organ Differentials

Leo Loeb, ***Washington University***

Varied series of transplantations of normal tissues and of tumors into the individuals in which the tissues originated, as well as into other individuals with different degrees of genetic relationship to the donor of the transplant, have led to the conclusion that each individual is characterized by an individuality differential, a substance which is the same in all or in the large majority of the organs, tissues, and cells of this individual and which differs from such substances in all other individuals. Corresponding substances characterize strains, races, species, genera, and classes of organisms. These various specific substances represent the organismal differentials. A piece of tissue or of tumor possessing a strange organismal differential, when introduced into a host, here calls for an antagonistic reaction on the part of the host cells, the most characteristic of which is the lymphocytic reaction which quantitatively indicates the degree of nearness or distance of the genetic relationship between host and transplant.

Within the same individual we may distinguish the different organs and tissues, such as kidney, liver, thyroid, skin, or cartilage, all of which possess the same set of organismal differentials, but differ in characteristics that are similar in the corresponding organs and tissue of all individuals, although in different individuals they possess different organismal differentials. These characteristics of various organs and tissues represent the organ and tissue differentials. In contrast to the organismal differentials, they do not as such elicit specific antagonistic reactions when transferred to other individuals. Both organismal differentials and organ differentials are associated in various ways in each individual, and they exert specific functions which vary in accordance with the prevalence of one or the other of these two types of differentials. It will be of interest to analyze in various vital processes the relative functions and preponderance of the organismal differentials and of the organ differentials, respectively.

The Quantitative Histochemistry of the Brain

Oliver H. Lowry
Washington University School of Medicine

The structural complexity of the brain is such that interpretation of gross biochemical data seems almost hopeless. Simplification has been attempted through histochemistry. Of the several histochemical methodologies available that of Linderstrøm-Lang and his collaborators, which is capable of providing direct quantitative information and is otherwise advantageous, was adapted to the present purpose. The necessary changes included (*a*) the use of frozen-dried material and (*b*) a drastic reduction in the scale of analysis (10- to 10,000-fold), since with brain it is usually difficult to isolate regions larger than a few micrograms in weight that are sufficiently simple in structure to repay analysis for histochemical purposes. In order to obtain information of a broad metabolic and structural character, methods have been elaborated for the measurement of 10 different enzymes, 4 lipid fractions, 4 phosphorus fractions, riboflavin, and chloride on the necessary microscale (5 μg dry weight or less). In some cases the methods are sufficiently sensitive for the analysis of single large cell bodies. These are weighed directly on a simple quartz balance before analysis (weight, about 0.02 μg). Illustrative data are presented.

On the Mode of Action of Glycerol in Preventing Injury by Freezing in Embryonic Tissues of Chick

B. J. Luyet and P. M. Gehenic
St. Louis University

Pieces of embryonic chick heart, previously immersed in glycerol, survive freezing in liquid nitrogen, as shown by their growth in tissue culture. To investigate the factors involved in that protective action, we determined what effect the immersion of the tissues for various lengths of time in various concentrations of glycerol may have in inducing longer or deeper supercooling, in preventing freezing, in reducing the amount of ice formed, and in permitting survival under these conditions. It was found that glycerol, besides dehydrating the tissues and lowering their freezing point, also delays the initiation of crystallization, retards the advance of the ice front through the tissues, and reduces the amount of ice formed at a given temperature. Furthermore, the treated pieces survived despite the formation of some ice in them. This latter finding indicates that the primary factor in the protective action of glycerol is not the prevention of, or the delay in, crystallization nor the lowering of the freezing point, but the ability of glycerol to reduce the amount of ice formed, an effect possibly attributable to some water-binding properties of glycerol.

Experimental Observations on the Role Played by Anaphylaxis in the Development of Renal Disease Following the Infusion of Mismatched Blood

A. D. Mason and C. Barber Mueller
Washington University School of Medicine

A series of dogs has been studied in regard to the production of renal disease following mismatched blood transfusions. Normal dogs can handle free dog hemoglobin in great quantities without evidence of renal tubular disease. Dogs normally hemolyze human blood as rapidly as it is infused and can dispose of the products of hemolysis without functional or pathological evidence of renal disease. If human blood is given to a dog about 4 weeks after a previous infusion, the dog shows a different type of response, characterized by cyanosis, collapse, vomiting, diarrhea, and shock. Subsequent to this infusion there is a persistent reduction in renal blood flow, with gradual recovery in most of the animals and a restoration of renal blood flow to normal values.

During the period of renal blood flow reduction there is elevation of the blood urea nitrogen. This returns to normal as the renal blood flow resumes normal values. If the renal blood flow has been reduced for a sufficient period of time, there is microscopic evidence of renal tubular disease, characterized by atrophy of the epithelium, dilatation of the tubules, and increase in interstitial fibrosis.

Reproductive Organs in Relation to Adrenal Cortex Secretions

Carl R. Moore, ***University of Chicago***

Pathological conditions in the adrenal cortex of man

and of some strains of mice have indicated that the adrenal cortex secretes sex hormonelike substances that have profound effects, but it is less clear that normal adrenal cortex produces substances that have an effect upon the reproductive system.

Whereas an embryonic testis of the rat, transplanted into the walls of seminal vesicles of castrated adults, actively secretes male hormones that stimulate immediately adjacent seminal vesicle epithelium to an adult secretory type, similar transplantation of embryonic or postnatal adrenal glands fails to evoke a corresponding reaction; the adrenal cortex does not secrete male hormonelike substances in sufficient quantity to be detected by this most sensitive indicator method.

Cortisone acetate (Merck), a secretory product of the adrenal cortex, injected daily into rats—male and female, normal and gonadectomized, immature and sexually mature—fails to reveal a malelike or femalelike substance or a gonad-stimulating substance.

Purified adrenocorticotrophin (Armour), which stimulates the secretion of active substances by the intact adrenal cortex, likewise failed to produce responses in the various types of rats that suggested male or female hormone responses, or a sex gland-stimulating substance.

Adrenalectomy of sexually mature males and females did not produce detectable effects upon reproductive tissues. Adrenalectomy, coupled with castration, in immature males had but slightly detectable effects upon accessory reproductive organs above that of castration alone; the slight effects were associated with subnormal nutritive states.

Since positive effects attributable to normal adrenal cortex secretions did not appear, it is suggested that those effects associated with pathological adrenals may perhaps be due to an abnormal synthesis of adrenal steroids by the cortex, which yielded substances having effects ordinarily attributed to sex hormones.

Absorption of Radioiron from Foods

Carl V. Moore and Reubenia Dubach
Washington University School of Medicine

Nutritional requirements for iron have not been established with precision, in part because it has been so difficult to determine how completely man absorbs the iron in food. The present study was designed to provide this information by measuring the assimilation of radioiron from foods by healthy human subjects, and by patients with hypochromic and pernicious anemia. The foods selected for study were those which could most easily be produced or grown so as to contain radioiron: eggs, chicken and rabbit liver, chicken muscle, mustard greens, and spinach. Results may be summarized as follows:

1. With very few exceptions, the absorption of Fe^{59} from these foods by healthy human subjects was less than 10%.
2. Iron-deficient subjects usually did not assimilate the food iron any more efficiently than did normal persons. Even when absorption was more complete, the difference was less striking than occurs after the feeding of inorganic iron salts.
3. Ascorbic acid and foods containing ascorbic acid enhanced the absorption of food iron. Other organic acids and reducing substances were less effective.
4. In patients with achlorhydria, it was not possible to increase the absorption of Fe^{59} either by therapeutic doses of 0.1 *N* HCl or by mixing enough 1 *N* HCl into the food prior to administration to lower the pH of the mixture to 1.5.

It is estimated that the normal adult male must assimilate between 0.5 and 1 mg iron/day in order to stay in balance. For the normal adult woman, the amount needed per day is probably 1.0–1.5 mg, depending on the menstrual loss of blood or the frequency of pregnancies. If only 10% of food iron is absorbed, it is clear that the recommended dietary allowances of 12–15 mg/day are none too high.

Studies of the Oxide Cathode

L. S. Nergaard, *RCA Laboratories Division, Radio Corporation of America*

Studies (1) of the decay and recovery of the pulsed emission of oxide-coated cathodes, (2) of the internal impedances within the cathode, and (3) of the effect of barium deposited on the surface of such a cathode by means of a mass spectrometer have led to a new physical model of the oxide-coated cathode. The salient features of this model are (1) the oxide cathode is an impurity semiconductor; (2) the donors are oxygen vacancies; (3) the donors are mobile—i.e., can diffuse and electrolyze readily at the normal operating temperatures of oxide cathodes, so that the internal conductivity of the cathode is a function of current. In this model, pulse decay results from donor depletion layer near the emitting surface of the cathode when high currents are drawn; recovery results from back diffusion of the donors. The model accounts for the anomalous Schottky effect of oxide cathodes and for other anomalous behaviors.

Hyperfine Structure in Paramagnetic Resonance of Free Radicals

G. E. Pake, J. Townsend, and S. I. Weissman
Washington University

Certain free radicals, in sufficiently dilute solution, exhibit a well-resolved hyperfine structure of the paramagnetic resonance line. The chemist is interested in this hyperfine structure because the magnitude of the splitting and the identity of the nucleus involved give information concerning properties of the wave function of the odd electron.

For the physicist, free radical systems provide examples par excellence of the phenomenon of exchange narrowing, and they serve as proving grounds for theories involving the interplay among exchange, magnetic dipole-dipole interaction between electrons, the electron-nucleus interaction responsible for hyperfine splitting, and thermal relaxation as mechanisms of line broadening. Experiments at Washington University raise questions as to the criterion for the appearance of hyperfine splitting, which does not always arise for dilute free radical solutions expected to show it, and as to the mechanism of broadening of the individual hyperfine structure components when they are resolved. These experiments have also led to the discovery of a free radical with static and resonant susceptibilities strongly suggestive of antiferromagnetic behavior.

The Sticking Coefficient of Nitrogen in Air and its Application to Low Pressure Measurement

K. L. Perkins, J. J. Ruddick, and A. H. Weber
St. Louis University

The sticking coefficient of air (mostly nitrogen) on

tungsten was measured in high vacuum by observing the time of deposition of a monolayer of the gas on the clean metal surface.

The *average* sticking coefficient α_{av} was measured as 0.14, and the initial sticking coefficient α_0 as 0.26. The latter value agrees reasonably with 0.3 obtained by Becker and Hartman. A new photoelectric measurement of α_0 is at present yielding a preliminary value of 0.39.

The measured sticking coefficients are applied in the measurement of low pressures. It is concluded that pressures below 10^{-7} mm Hg can be measured reliably.

Spectral Studies in the Far Infrared

K. S. Pitzer, W. D. Gwinn, J. L. Hollenberg, and C. Bohn, *University of California, Berkeley*

A grating spectrometer has been built and operated satisfactorily in wavelength range 25–70 μ. The spectrum of water vapor was measured as a calibration and test. This spectral region contains important bands arising from bending vibrations of molecules. In some cases these frequencies can be found in the Raman spectrum, but in other cases the selection rules allow certain frequencies only in the infrared. Results are presented for 1,2-dichloroethane and several other halogen derivatives of ethane or ethylene. By completing the vibrational assignments for such molecules, it will be possible to draw valid conclusions concerning thermodynamic properties and interatomic forces within molecules.

Double Beta Decay and Theories of the Neutrino

H. Primakoff, *Washington University*

The present theory of elementary particles is consistent with the existence of (*a*) neutrinos and their antiparticles—antineutrinos—or (*b*) neutrinos alone. In case (*a*), neutrino and antineutrino are in principle distinguishable through the sign of their magnetic moment—the expected magnitude of the moment is, however, extremely small. Experimentally, the question of the existence of antineutrinos may be studied by investigation of the phenomenon of double beta decay—the spontaneous disintegration of a nucleus of mass number A, charge number Z, into one of mass number A, charge number Z + 2. Theory shows that, if antineutrinos exist, (1) the two emitted electrons are accompanied by two emitted antineutrinos, and (2) the mean life of the decay is much longer than if antineutrinos are absent. Moreover, if antineutrinos do not exist, the two decay electrons are emitted unaccompanied by neutrinos, so that their total kinetic energy is the same for all individual disintegrations; the angular correlation function of the electrons has been calculated in this case and turns out to be $\sim 1 + \cos \Psi$ in the most readily observable situations.

The available experimental results still do not distinguish between the two major possibilities outlined; the preponderance of present evidence, however, seems to favor the existence of antineutrinos. A review of recent results is given and implications are drawn in addition regarding the probably related process of μ-meson decay.

The Propagation of Certain Short-Period Air Pressure Oscillations Recorded by the Macelwane Microbarograph

Walter H. Roschke, Jr.
St. Louis University* and *Parks College

The investigation of 29 air pressure microoscillations of the impulse type with a period of 10–25 sec, as recorded by Macelwane Electromagnetic Microbarographs in a tripartite arrangement (dimensions: 45, 63, and 65 ft), at Florissant, Missouri (near St. Louis), during May and June 1950, reveals that these oscillations are propagated in the direction and with a speed that is of the same order of magnitude as the wind speed in the lower layers of the atmosphere, but not necessarily at the surface.

The Nuclear Interactions of μ-Mesons

R. D. Sard, *Washington University*

Although the μ-meson has relatively weak coupling with nucleons and gives them but little energy in interacting, its appearance in the decay schemes of the π- and K-mesons makes it certain that a detailed knowledge of its nucleonic interactions will be of great value in finding a satisfactory theory for the whole family of unstable particles produced in high-energy nuclear collisions. A survey is given of present knowledge of the μ-meson nuclear interactions, in the course of which results obtained recently at Washington University are reported.

An Invariant Force Function in Muscle Activity

Gordon M. Schoepfle, William W. Sleator, Jr., and Arthur S. Gilson, Jr.
Washington University School of Medicine

The simple twitch constitutes the basic element of response of a muscle fiber to any single suprathreshold stimulus. The extent to which a muscle shortens transiently during a twitch against a constant load is decreased as the load is increased, but the time parameters of the contraction phase are very nearly independent of load or shortening in unfatigued muscle. If a small weight Δw is removed from the constraining load on the resting turtle neck retractor, the muscle will shorten through a length ΔL. The ratio $\Delta L/\Delta w$ is proportional to extent of shortening at any given time during the contraction phase, regardless of load or extent of shortening. The proportionality factor has the dimensions of a force and may be formulated as a force time function $f(t)$, invariant for all twitches against a constant load, regardless of load or extent of shortening.

Total tension is constant throughout the system in the case of this slowly acting muscle, but a structural reorganization of the system during activity may be thought of as leading to a redistribution of force components such that one of them becomes manifest in determining $f(t)$. These data are consistent with the "transmutation chain" theory of Buchtal and Kaiser, in which the fiber is assumed to consist of parallel molecular chains, each link of which exists either as an elongated element or as a shortened element. Some of the shortened elements may be fixated by a special substance liberated in constant amount during each twitch.

Chemical Control of Hypertension

Henry A. Schroeder, H. Mitchell Perry, Jr., and John D. Morrow
Washington University School of Medicine

Arterial hypertension is mediated by the interaction of at least two influences (1) neurogenic, dependent upon the vasoconstrictor mechanism of autonomic nerves; the chemical effector substances are acetyl choline for gangli-

onic transmission and *nor*-epinephrine for neuromuscular transmission; (2) nephrogenic, initiated by renal ischemia and dependent upon pherentasin and probably other primary amines in blood. The state of hypertension can be reversed, therefore, only by antagonizing both influences simultaneously. In more than 200 patients benefit has been accomplished.

Hexamethonium chloride is used to block ganglionic transmission. Given orally, it causes partial paralysis of autonomic nerves. 1-Hydrazinophthalazine is used to inactivate pherentasin; a carbonyl reagent, it apparently combines with the carbonyl group in pherentasin, as well as with other carbonyl compounds, such as pyruvic acid. It also has an affinity for sulfhydryl compounds both *in vivo* and *in vitro* and for heavy metals *in vitro*.

Many of the secondary effects of increased intra-arterial tension are reversed, especially congestive heart failure, low-grade renal insufficiency, angina pectoris, and the signs of the malignant stage. Rapid excretion or destruction of both drugs requires frequent administration.

The Significance of the Two Components of the Pain Path in the Surgical Relief of Disordered Sensibility

Henry G. Schwartz and James L. O'Leary
Washington University School of Medicine

To select the procedure offering the most promise of relief of unremitting pain is an aspect of neurosurgery requiring precise interpretation of the disordered sensibility. Among the conditions giving rise to such unremitting pain are neuralgias, causalgias, a phantom limb, tabetic crises, and malignant growth. Procedures available are paravertebral nerve block, section of nerve roots next the spinal cord, section of pain tracts in the cord, and frontal lobotomy. The character and distribution of the pain indicate the procedure of choice.

Recent studies by Bishop and Landau support prior evidence that there are two kinds of pain. Pricking pain, which is conducted centrally from the skin over small myelinated peripheral axons with fusion at 30/sec stimulation, may be blocked differentially in man by a pressure cuff about the arm. After blocking, a burning pain of long latency can still be elicited, with fusion at 3–5/sec. This pain is believed the same as that shown by Gasser and Hughes to be conducted over nonmyelinated axons, and is closely akin to that identified by patients as unremitting pain.

In our study we have used the conventional procedures of cutaneous stimulation on patients, studying the two pain components before and after section of the pain paths in the spinal cord. Our present results indicate that both pricking and burning pain follow the same route to higher centers. Other evidence from experimental animals suggests that the two pain components also relay in the same region of the thalamus.

The results are considered in the light of past contributions by Head and by Trotter and Davies.

The Nature of Kinetic Barriers in Aqueous Reactions

Philip A. Shaffer
Washington University School of Medicine

In a search for clues to the nature of factors that restrain the spontaneous velocities of many dynamically permissible reactions ("kinetic barriers"), the writer examined some years ago a number of oxidation-reduction reactions between reversible ionic couples. In the form of galvanic cells these reactions exhibit no evidence of "latent resistance" to reaction rate, except that inherent in the "electro-chemical apparatus;" but in homogeneous solution some are slow or unreactive in the absence of catalysts or mediators. Examination of the latter group revealed several factors reported briefly as hypotheses in 1933, 1936, and 1939.

More recently this study has been resumed. It now seems probable that at least three distinguishable factors may be identified.

1. Like sign of electrical charge of reactants (coulombic repulsion) may alone suppress reaction when $-\Delta F$ is relatively low.
2. The "equi-valence-change" principle (suggested in 1933) may alone suppress reactivity. Both (1) and (2) may be mediated in several ways.
3. In many cases participation of *both* ions of *water* —the ionization of $(H_2O)_n$—seems essential. This is perhaps a major factor in the "energy (heat) of activation" as measured by temperature coefficients.

Data for a few reactions are presented to illustrate the separate influences of these factors controlling reaction rates; they may be dominant factors of more general applicability to this complex problem.

The Electroyltes of the Endolymph and Perilymph

Catherine A. Smith, Mei-Ling Wu, and Oliver H. Lowry
Washington University School of Medicine

By using a special surgical approach it is feasible to obtain about 0.5 mm^3 (.0005 ml) of endolymph and 1 or 2 mm^3 of perilymph from the ear of a guinea pig without appreciable contamination or evaporation. These fluids, together with spinal fluid and blood plasma, were analyzed for Cl, Na, and K, using analytical procedures that had to be developed specifically for this purpose because of the minute amounts of fluid available. Perilymph proved to be nearly identical with spinal fluid in regard to the 3 anions measured. Endolymph, however, was found to have a K concentration 20 or 30 times that of perilymph (140 mEq/l compared to 6) and a Na concentration only a tenth as high as perilymph or spinal fluid (15 compared to 150 mEq/l). The Cl of endolymph is 90% of that in perilymph and spinal fluid. Endolymph has thus proved to be unique among known extracellular fluids, and it seems possible that its unusual electrolyte pattern is implicated in the function of the special sense organs concerned.

Properties of Myelinated Fibers in Sciatic Nerve and in Spinal Cord (Frog) as Examined with Microelectrodes

Ichiji Tasaki, *Central Institute for the Deaf*

This investigation aims to clarify the properties of the myelinated nerve fiber by introducing capillary microelectrodes into individual nerve fibers. Action potentials were recorded through such a microelectrode inserted in various parts of an isolated nerve fiber and were compared with the action current records taken simultaneously from the same internode of the fiber. With the electrode

inserted in the innermost layer of the myelin sheath but still outside the axis cylinder, action potentials of 1–30 mv were observed, but there was no measurable resting potential. Conduction across the impaled region was not hindered by this procedure. When the microelectrode was introduced into the axis cylinder, either in the internode or at the node, both resting and action potentials were observed. Both were generally less than 30 mv. The action currents indicated that the response of the fiber was reduced by the injury caused by introduction of the electrode. Conduction across the impaled internode failed within 1–10 min after the appearance of a resting potential had indicated that the electrode had entered the axis cylinder. Conduction could be restored by passing an inward-directed electric current through the internal electrode.

Isolated single fibers were excited by brief pulses of current applied through microelectrodes at various parts of the fiber. The surface membrane at the node of Ranvier is the only place where stimulating (outward-directed) current can induce a response.

Action potentials from individual fibers in the spinal cord were recorded with microelectrodes inserted into individual fibers. By applying polarizing currents through such an internal electrode, physiological evidence was secured for the existence of the nodes of Ranvier in the fibers in the dorsal funiculus.

The threshold for a single fiber in the dorsal funiculus was measured by observing the responses in single (afferent) fibers in the muscle nerve. The threshold varied greatly from point to point along the course of the fiber. The nodes of Ranvier of the fiber could be located by this method.

The Composition of the Stony Meteorites and the Abundances of the Elements with Particular Reference to Iron

Harold C. Urey and Harmon Craig

University of Chicago

The iron and achondritic meteorites represent highly differentiated materials, and unless their origin is well understood they cannot be used for determining the composition of cosmic matter. The achondrites can be classified into two groups—namely, those having a composition similar to basalts and those having silicates of the same composition as the silicate phase of chondrites. The latter appear to be overheated chondrites. The chondrites, because of their thoroughly mixed-up structure, may represent an average sample of the colliding asteroids that produced them. The chondrites, on the basis of selected analyses, contain two prominent groups having markedly different amounts of total iron, so that some fractionation process has partially separated the silicate and iron fractions, just as has occurred in the case of the terrestrial planets. Possible separation processes are discussed. It is concluded that the lower abundance of iron is more probable, and from our data iron has an atomic abundance of ~ 0.6 that of silicon.

On the Theory of Bernoulli Numbers

H. S. Vandiver, *University of Texas*

The numbers of Bernoulli, which are used in many parts of mathematics, consist of a certain infinite set of rational numbers, which numbers are usually designated by B_k, where k ranges over the set of positive whole numbers, and they may be conveniently defined by a certain algebraic recursion formula. For more than a century mathematicians have been studying the arithmetical properties of the numerators and denominators of the B's; some of the principal results that have been discovered along this line, particularly several of the recent ones, are explained. Some of these turn out to be related to a few of the deepest outstanding questions in the theory of numbers.

Gene Action in Connection with Growth and Development

F. W. Went, *California Institute of Technology*

Theories on gene action are largely based on their effects on biochemical synthesis. Work, particularly on adaptive enzymes, indicates that genes initiate but do not quantitatively control such syntheses. Yet, for the genetic control of growth and development, mechanisms are indicated that control growth to within a fraction of 1%. Reproducibility of growth under controlled conditions is much greater than originally suspected and requires special consideration in connection with genetic control. One mechanism that satisfies the requirements for quantitative control of growth, with even self-regulatory features, is a diffusion process limiting nuclear-cytoplasmic interaction. This idea is developed in connection with some new facts about plant growth.

Mechanism of Adrenal Hyperplasia and Androgenicity

Emil Witschi, *State University of Iowa*

Adrenal hyperplasia, often combined with virilism, is a relatively frequent morbid condition in young men and women. For an analysis of its etiology it is fortunate that a similar adrenogenital syndrome can be experimentally induced in frog larvae, through treatments with estrogenic steroid hormones. By high dosages the adrenal tissue is increased tenfold, and the gonads of genetically female larvae are transformed into hermaphrodite glands or testes. However, the masculinization does not represent a direct response of the sex gland to the estrogen, but is mediated through the adrenal glands.

Moreover, if larvae were hypophysectomized before initiation of the hormone treatment, the adrenals do not enlarge but remain just as underdeveloped as in hypophysectomized controls. A complicated hormonal reaction chain is thus revealed, of which even now we know only some major links. In general we recognize the following sequences: The high estrogen concentration apparently depresses the gonadotropic component of the hypophyseal function complex, which in turn leads to an increase in ACTH production and subsequent adrenal hyperplasia. It is not known whether a hyperplastic adrenal is hyperfunctional in a general sense or whether some of its minor capacities increase disproportionately; but the experiments show that at a certain level the hormonal secretions reach an androgenic threshold value, which in frogs is sufficient to dominate even the sexual differentiation of the gonads.

A brief discussion of the mechanism of hormonal reaction chains is given.

Ion Exchange between Alkali Halide Crystals under the Fusion Temperature

Lyman J. Wood, *St. Louis University*

In the past fine powders have been largely used in studies of reactions between solids. Several alkali halides can now be had in the form of large crystals, and the investigation of such problems as (*a*) the thickness of the initial reaction layer, (*b*) the rate of penetration of ions into solid crystals, and (*c*) ion exchange at the surface can now be greatly simplified. Because of its unique character the reciprocal system $RbCl + KBr \rightleftharpoons RbBr + KCl$ was selected for detailed study. It has now been shown that this reaction occurs at temperatures far below the fusion point. By the use of a macrocrystal of potassium bromide reacting with fine rubidium chloride powder, at below fusion temperatures, it has been possible to show that (*a*) rubidium chloride vapors react rapidly with the surface of the potassium bromide, (*b*) after the comparatively rapid initial surface reaction the rubidium and chloride ions continue to penetrate into the potassium bromide crystal but at a decreasing rate, (*c*) all the potassium, rubidium, bromide, and chloride ions are contained in one solid solution. The formation of this sort of solution is not only interesting in itself but makes possible a subtle combination of the refractive index and x-ray methods of analysis. By a combination of these two analytical methods it was possible to distinguish between ion migration through the crystal and transfer in the vapor phase along accidental faults. Rates of penetration into the crystal were found to decrease greatly as the temperature decreased further below the fusion point.

Surface Phagocytosis

W. Barry Wood, Jr., and Mary Ruth Smith
Washington University School of Medicine

Man's ability to recover from acute bacterial infection depends in large measure upon the leucocytes that are formed in his bone marrow and circulate in his blood. In the presence of infection these cells pass through the walls of the blood vessels and accumulate at the site of bacterial invasion. There they phagocytize the bacteria and destroy them. Certain microbes that cause serious infections, however, are able to resist ingestion by virtue of outer capsules that protect them from the phagocytic cells. If the host is able to survive the infection for 5 or 6 days, his tissues will make antibodies which react with the capsules of the bacteria and render them susceptible to phagocytosis. Since antibody production is a slow process, survival in the early stages of infection depends upon destruction of the bacteria in the absence of antibodies. Leucocytes have been shown to destroy encapsulated microbes in the crucial preantibody stage of infection by a process referred to as "surface phagocytosis." Its occurrence *in vitro* and in the blood stream of rabbits with bacteremia has been recorded by motion picture photography.

A Biometric Analysis of Natural Selection in *Asclepias tuberosa*

Robert E. Woodson, Jr., *Washington University*

Asclepias tuberosa, popularly known as butterfly weed and orange milkweed, consists of four subspecies, two of which are allopatric in the eastern United States. Of particular interest are the remaining two subspecies, which apparently are sympatric and with a common center of distribution in the Ozark highlands of Missouri. The constituent populations radiate roughly in a vast semicircle from near Toronto on the northeast to Monterey on the southwest and to the Black Hills on the northwest; both subspecies merge toward the southeast with the allopatric eastern subspecies.

The populations of the Ozarks, which are typical of ssp. *interior*, were first distinguished from those of the far periphery, typical of ssp. *terminalis*, through the shapes of their leaf bases, which are cordate and more or less cuneate, respectively. In the intervening area the population means of the leaf bases gradually merge from one to the other extreme, creating a striking series of concentric isophenes when plotted upon a phenocontour map.

Biometric analysis indicates that the two subspecies are interfertile and that ssp. *interior*, the younger of the two, is penetrating and obliterating the surrounding populations of the older ssp. *terminalis* through introgressive hybridization. The secret of the genetic success of ssp. *interior* apparently is its associated reproductive potential and general vigor, which are considerably greater than those of ssp. *terminalis*.

The implementation of natural selection by introgressive hybridization, termed "sabinism," is discussed briefly.

Electric Response of the Retina to Change of Color

Alexander Forbes and Sylvia Burleigh
Harvard University

Onset and cessation of illumination both evoke electric responses in vertebrate retinas. If, without change in intensity, shift from one color to another evokes electric response, it relates the potential to color discrimination. A beam-splitter brought two light beams to coincidence on the retinas of frogs or turtles. Interference filters delivered nearly monochromatic light—red, yellow, green, or blue. A beam-shifting shutter made the transition between colors with minimum flicker. Intensities were balanced with rheostats in the lamp circuits. With all six combinations of these colors the shift evoked electric responses; no balancing of intensities abolished it. The response in long-wave-to-short-wave shift differed from that in the reverse shift. In the dark-adapted frogs, when the beams were equivalent as judged by the "b-wave" (positive), the preceding "a-wave" (negative) was absent or small and brief in the short-to-long-wave shift, larger in the reverse shift. The b-wave showed longer duration in short-to-long-wave shift than in the reverse. Frogs have both rods and cones whose differential involvement might explain the differences in responses to different colors. Yellow and blue with light-adapted frogs showed reversal of the above differences. Turtle retinas (only cones) showed shift responses with less difference between short-to-long and long-to-short shifts than in the frog. The slight differences more nearly resembled those in light-adapted than in dark-adapted frogs. Rod-cone differential may therefore explain some, but not all, features of the responses.

News and Notes

Scientists in the News

John A. Behnke, formerly with W. H. Freeman & Co., San Francisco, has joined the staff of the AAAS as assistant administrative secretary. With 23 years in the publishing business, successively with the Macmillan Co., W. B. Saunders, and Freeman, Mr. Behnke has had nationwide contacts with scientists in many fields. The Association will make use of his background in developing and strengthening its relations with affiliated and associated societies, including the academies of science, and it is also planned to have Mr. Behnke take charge of the publication of the Association's symposium series.

Don S. Burrows, of Arlington, Va., has been appointed controller of the U. S. Atomic Energy Commission. Mr. Burrows, who left the Reconstruction Finance Corporation to take the AEC position, succeeds **Lindsley H. Noble,** who resigned to become controller of the Panama Company.

Joseph S. Butts has been granted leave of absence from Oregon State College to accept a position in the Division of Biology and Medicine of the Atomic Energy Commission.

P. A. Chieri has resigned as associate professor in mechanical engineering at Newark College of Engineering, Newark, N. J., to serve as professor of mechanical engineering and head of the Mechanical Engineering Department at Southwestern Louisiana Institute, Lafayette.

Charles A. Domenicali has joined the technical staff of the Solid State Physics Division, Franklin Institute Laboratories for Research and Development in Philadelphia. Dr. Domenicali was a former associate professor at Alfred University, Alfred, N. Y.

L. Kraeer Ferguson, professor of surgery at the Woman's Medical College of Pennsylvania, has been appointed director of the Surgery Department at the Frankford Hospital in Philadelphia.

Anna Freud, of Cambridge, daughter of the late Sigmund Freud, has accepted a post at Harvard University, where she will serve as consultant to the School of Education's Laboratory of Human Development.

Harry H. Goode has been made director of the Willow Run Research Center, University of Michigan. He was previously supervisor of the Aerophysics Department and chief project engineer.

Clarence H. Graham, of Columbia University, has been appointed psychologist attached to the London office of ONR. He will be in London for a period of 11 months. During the past summer he was professor of psychology in the Kyoto Seminars in American Studies, which were conducted under the sponsorship of the University of Kyoto, Doshisha University, the University of Illinois, and the Rockefeller Foundation.

B. J. Kennedy, formerly of the Massachusetts General Hospital in Boston, has been appointed assistant professor in medicine at the University Hospitals, University of Minnesota Medical School, Minneapolis. In this position he will act as director of the Department of Metabolism and the Section of Cancer Medicine.

Woodrow B. Kessler, formerly of the University of Texas, Dental Branch, Houston, is now with the Department of Physiology, Vanderbilt University School of Medicine, Nashville, Tenn.

Alvin I. Kosak has been appointed assistant professor of industrial medicine at the New York University Postgraduate Medical School. He was formerly assistant professor of chemistry at the University of Cincinnati.

Otto E. Lobstein, formerly of Northwestern University Medical School, is now associated with S. I. Dulkin, of the Chem-Tech Laboratories, Beverly Hills, Calif. Dr. Lobstein will direct the clinical research division of this laboratory, extending the consulting services offered to hospitals and clinical laboratories.

The New York City branch, American Association of University Women, has presented its annual Woman of the Year in Education Award to **Millicent C. McIntosh,** president of Barnard College.

Howard O. McMahon, science director of Arthur D. Little, Inc., received the Frank Forrest Award for 1952, at the fall meeting of the American Ceramic Society, Glass Division. The award is given annually by Frank W. Preston and the Preston Laboratories in memory of Frank Forrest, of the Preston Laboratories, to encourage others to publish papers on glass technology. Dr. McMahon received the award for papers published in the *Journal of the American Ceramic Society.*

S. M. Marco has been named chairman of the Department of Mechanical Engineering at Ohio State University, succeeding **Aubrey I. Brown,** chairman since 1946, who asked to be relieved of the chairmanship to devote his time to teaching.

George Burke Maxey, assistant professor of geology at the University of Connecticut, is on a year's leave of absence serving as technical adviser, geologist (Water Resources), to TCA, with headquarters at Tripoli. He will conduct a general survey of the water resources of Libya upon which to base recommendations regarding development of the country's water supplies and formulation of policy for water conservation. His university duties have been assumed by **Paul Tasch.**

Richard L. Meiling, associate dean and associate professor of gynecology and obstetrics in the Ohio State University College of Medicine, recently addressed the 29th Congress of the German Society of Gynecology in Munich, reviewing the work done in recent years at University Hospital by staff members of OSU's departments of radiology, medicine, obstetrics and gynecology, and pathology in the treatment of cancer of the cervix with radioactive cobalt. While in Europe Dr. Meiling will visit the USAF hospitals in his capacity as medical consultant to the Secretary of Defense and the Surgeon General of the Air Force.

Lewis H. Rogers has been appointed head of the Division of Analytical Chemistry of National Dairy Research Laboratories, Inc., Oakdale, N. Y. Dr. Rogers has been in charge of an analytical research group in a division of Union Carbide and Carbon Corporation operating at Oak Ridge, Tenn., under AEC auspices.

Jerome F. Saeman, research chemist in charge of work in cellulose and wood chemistry at the U. S. Forest Products Laboratory, has left Madison, Wis., for Lucknow, where he is representing the U. S. in conferences on the production and use of alcohol for power. He is on special assignment with FAO.

Edmund M. Spieker, chairman of the Department of Geology at Ohio State since 1944, has been appointed a research professor in the department. He has been a member of the faculty since 1924. **Carl A. Lamey,** who joined the staff in 1935, has been appointed geology chairman to replace Dr. Spieker.

Phillip H. Starr, instructor in psychiatry at the Washington University School of Medicine, has been appointed acting director of the Washington University Community Child Guidance Clinic. Dr. Starr will continue as chief psychiatric consultant to the St. Louis Children's Hospital and as director of the Children's Mental Health Clinic.

George H. Whipple, Nobel prize winner in medicine, has resigned as dean of the School of Medicine and Dentistry at the University of Rochester. Dr. Whipple plans to continue on the staff as a professor of pathology.

Abraham White, vice president and research director of Chemical Specialties Co., has been appointed associate director of the new College of Medicine sponsored by Yeshiva University. Dr. White will also serve as chairman of the new medical school's Department of Biochemistry and will continue to serve as Chemical Specialties' vice president and scientific adviser.

Gardner P. Wilson has joined Consolidated Engineering Corporation as a senior development engineer and will be in charge of the Mass Spectrometer Group of the Engineering Department. From 1945 to 1952, Mr. Wilson was head of the Test Division of the U. S. Naval Ordnance Test Station, Pasadena.

Education

Hahnemann Medical College has appointed B. Marvin Hand professor and head of the Department of Neurology, and Van B. O. Hammet professor and head of the Department of Psychiatry.

The **Université de Montréal** has appointed Marcel Bourgon assistant professor of inorganic chemistry, and Henri Favre, of the Institute of Technology, Zurich, assistant professor of organic chemistry. Dr. Favre's research will be on Canadian natural products containing terpenes and alkaloids.

Coincident with the first graduation ceremony of the **New South Wales University of Technology** at Sydney, Australia, which was opened in 1950, announcement was made of the appointments of A. H. Willis to the newly created Nuffield research chair of mechanical engineering; R. H. Myers to the chair of metallurgy; and C. J. Milner, formerly head of the Physics ection of the British Thomson-Houston Research Laboratory, to the chair of applied physics.

Stevens Institute of Technology has promoted J. Myron Johnson to assistant director of its Laboratory of Psychological Studies. Joseph G. Phelan has been appointed assistant professor of psychology.

Recent visitors at the **University of Texas** Medical Branch, Galveston, were Pietro de Nicola, of the University of Pavia, who gave a series of special seminars; and Wolfgang von Heubner, of the Free University of Berlin, who gave a lecture on "Methemoglobin Formation," and discussed the organization of the medical education program in West Germany.

Grants and Fellowships

The **American Institute of Nutrition** invites nominations for the Osborne and Mendel Award of $1000, established by the Nutrition Foundation, Inc., for the recognition of outstanding accomplishments in general research in the science of nutrition. P. Handler, Department of Biochemistry, Duke University School of Medicine, Durham, N. C., is chairman of the nominating committee, which will consider nominations from any source. The institute also administers the $1000 Borden Award in Nutrition, established by the Borden Company Foundation, Inc. L. T. Samuels, Department of Biochemistry, University of Utah College of Medicine, Salt Lake City 1, is chairman of the nominating committee. Both awards will be presented at the annual meeting of the institute next spring, and nominations must be in the hands of the committee by *Jan. 1.*

The **Fund for the Advancement of Education** is offering approximately 250 Faculty Fellowships for 1953–54 to college teachers throughout the U. S. Each grant is approximately the equivalent of the salary of the recipient, plus certain expenses, and candidates should be between 30 and 45 who have been teaching for several years. All candidates must

be nominated by their respective institutions, and applications are returnable by *Jan. 10*. Chairman of the 15-member Committee on Faculty Fellowships is William DeVane, of Yale. Full information may be obtained from the committee, 575 Madison Ave., New York 22.

The **Health Information Foundation** has supplied the funds for a one-year study of Negro health practices in Southern rural communities, to be conducted by Tuskegee Institute. Ernest E. Neal, director of Tuskegee's Rural Life Council, will be in charge of the research, a report of which will later be published for distribution to health and community leaders.

The **James F. Lincoln Arc Welding Foundation** annual engineering undergraduate awards went to engineering students in 23 different schools. First award of $1129 was presented to Richard Cheverton and Thomas Musslewhite, of Georgia Institute of Technology, for their joint design of a subcalibre mount for a recoilless rifle. Scholarship funds of $1750 were also awarded to three schools in honor of the first three winners. The sixth annual competition closes on *June 29*. For full information, address the foundation at Cleveland 17, Ohio.

In the Laboratories

American Electronic Mfg., Inc., recently organized in Los Angeles, has elected Donald Lincoln Herr president. The new corporation, which is now making synchros, induction potentiometers, and servo motors, is building a manufacturing, research, and development plant for large-scale production. Serving as technical advisers to the company are C. S. Draper, E. A. Guillemin, and Y. J. Liu.

California Texas Oil Company, Ltd., has appointed G. W. Orton resident director of its affiliated companies in the United Kingdom. Mr. Orton will coordinate the activities of the Caltex affiliates in England and will also serve as director on the board of the Regent Oil Company, Ltd.

B. F. Goodrich Chemical Company has appointed T. B. Nantz manager of its new $5,000,000 vinyl plastic monomer plant under construction at Calvert City, Ky. Mr. Nantz has recently been engaged in the job of reactivating the government-owned West Virginia GR-S plant.

Gulf Oil Corporation has named Hollis D. Hedberg chief of the Geology and Geophysics Section of the Production Department; Robert L. Boggs has been made assistant to the department vice president; H. J. Wharton has been named chief exploitation engineer; and A. H. Stoecker has been appointed chief of the Economics Section.

National Chlorophyll & Chemical Co. has begun construction at Lamar, Colo., of a $1,000,000 plant for continuous extraction of chlorophyll. The company is a newly organized subsidiary of National Alfalfa Dehydrating and Milling Co., of which J. C. Hearn is president. John C. Kephart is vice president in charge of research.

The National Institutes of Health have expanded their visiting scientist program, under which research workers are invited to conduct their investigations in the USPHS laboratories for periods ranging from a few weeks to two years. First visiting scientist to be appointed under the new program is Horace A. Barker, of the University of California, who will collaborate with Arthur Kornberg, of the National Institute of Arthritis and Metabolic Diseases, upon the isolation of enzymes.

The Office of Naval Research has contracted with the following universities for support of research investigations: University of Tennessee, John M. Woodward; Syracuse University, M. W. Jennison; University of North Carolina, Milton M. Huppert; Miami University, Murray Sanders; University of Colorado, John W. Berry; University of Maryland, Edward Steers; Iowa State, F. G. Smith; and University of Pennsylvania, Harry E. Morton.

Meetings and Elections

The American Association of Scientific Workers has elected Harry Grundfest president, William F. Hewitt, Jr., secretary, and Leland H. Taylor treasurer. Vice presidents are Isidor Fankuchen, Linus C. Pauling, William H. Pearlman, Melba N. Phillips, Theodor Rosebury, and Catherine J. Witton.

The American College of Cardiology will hold a meeting Dec. 9 at the New York Academy of Medicine at which Lester Blum, Samuel J. Megibow, and William M. Nelson will discuss "Problems in Exclusion of the Mammalian Heart—Applications to Cardiovascular Surgery;" Robert A. Nabatoff will speak on "Resection of the Left Auricular Appendage for Recurrent Arterial Embolization;" and Aaron N. Gorelik will outline "Results of Cardiopericardiopexy for the Treatment of Rheumatic Heart Disease." Simon Dack will preside.

The American Phytopathological Society has elected the following officers: president, J. G. Dickson; vice president, J. H. Jensen; secretary, S. E. A. McCallan; treasurer, Saul Rich (three-year term). President-elect is G. F. Weber. The next annual meeting will be held with the American Institute of Biological Sciences at Madison, Wis., in September 1953.

Friends of the Armed Forces Medical Library have been organized with Henry R. Viets, of Boston, as chairman, and Robert M. Stecher, of Cleveland, as secretary-treasurer. Purpose of the Friends is to promote knowledge of, and interest in, the functions, resources, and services of the library and to support programs for its development. The old Association of Honorary Consultants to the Army Medical Library, Inc., is in the process of dissolution.

Miscellaneous

In cooperation with the **American Geographical Society**, Victor von Hagen will direct an intensive two-year study of the 12th-century Inca Highway. Mr. von Hagen will leave Dec. 1 for Lima, which will be expedition headquarters. After making preliminary preparations he will be joined in early February by eight permanent staff members.

To celebrate the centenary of the **American Pharmaceutical Association**, Chester G. Fisher, of Fisher Scientific Company, gave the association new electronic instruments and equipment to bring greater speed and accuracy to the preparation of the *U. S. Pharmacopoeia* and the *National Formulary*

The **Building Research Advisory Board** of the National Research Council has appointed the following new members for 1952–53: Miles Colean, J. R. Meehan, C. H. Topping, and Alfred T. Waidelich. A new BRAB rotation policy involves the appointment of six new members each year.

The library of the **University of Missouri** will furnish, on request, microfilms of *Die histochemischen und physiologischen Arbeiten von Friedrich Miescher* at $3.50 for a complete microfilm. This book, of which only a few copies are available, was compiled by Miescher's friends after his death and was published at Leipzig in 1897 by F. C. W. Fogel.

The **National Academy of Sciences—National Research Council** has begun a third survey of food and nutrition research in the U. S. under contract with the Department of Agriculture. The survey will follow the plan of earlier surveys and in addition will include suggested food and nutrition research projects in areas where further work is indicated.

The **Southern Association of Science and Industry** has presented its 1952 press award for outstanding journalistic work to John N. Popham, Southern regional correspondent of the New York *Times*. The annual prize of $100 and a certificate are given on the basis of distinguished news work contributing to industrial and scientific progress in the South.

The **Special Map Projects Section** of the U. S. Geological Survey has been abolished. The section functions—preparation of the state base map series, the millionth scale map, the 1:250,000 series, and other small-scale maps—have been transferred to the four regional offices of the Topographic Division. A small Scale Compilation Unit has been established in the Cartography Section of each region to accommodate this work, and the drafting and editing operations have been integrated with existing drafting and editing units.

Recent Deaths

George N. Bauer (80), mathematician, Portsmouth, N. H., Oct., 13; **Fred S. Carver** (—), of Short Hills, N. J., mechanical engineer, Portland, Me., Aug. 15; **Richard D. Chase** (82), civil engineer, New Bedford, Mass., Oct. 19; **Monroe G. Cheney** (59), geologist, Coleman, Tex., Sept. 27; **Charles H. Chetwood** (86), genito-urinary specialist, New York, Oct. 15; **Niels A. Christensen** (87), inventor, Cleveland, Oct. 5; **John D. Currence** (53), of Bernardsville, N. J., internist, New York, Oct. 20; **Robert W. Curtis** (83), chemist, Lakeville, Conn., Sept. 29; **Margaret Donohue Howell** (72), dentist, Norwalk, Conn., Oct. 4; **Mabel R. Fernald** (69), psychologist, Cincinnati, Oct. 9; **Luis A. Gomez** (62), surgeon, Bucaramanga, Colombia, Oct. 17; **David H. Goodwillie** (65), mechanical engineer, Toledo, Ohio, Oct. 17; **William E. Gye** (68), cancer researcher, Perth, Australia, Oct. 14; **Louis P. Hall, Jr.** (63), engineering designer, Morristown, N. J., Oct. 17; **Edward M. Hanrahan** (59), plastic surgeon, Baltimore, Sept. 30; **John H. Hardin** (86), former vice president, American Optical Company, Pasadena, Calif., Sept. 21; **William H. Hawkes** (93), metallurgist, New York, Oct. 13; **Edson B. Heck** (61), internist, New York, Sept. 25; **Walter L. Hervey** (90), educator, New York, Oct. 14; **Joseph C. Husslein** (79), sociologist, St. Louis, Oct. 19; **Richard V. Hyland** (57), consulting engineer, Southhampton, N. Y., Sept. 20.

Minas Joannides, Sr. (57), surgeon, Chicago, Sept. 8; **Adrian V. S. Lambert** (80), thoracic surgeon, New York, Oct. 15; **Nathan Levinson** (54), electrical engineer, Burbank, Calif., Oct. 18; **Harold E. McComb** (65), geophysicist, Washington, D. C., Oct. 11; **Thomas H. McInnerney** (85), of National Dairy Products Corporation, Greenwich, Conn., Sept. 30; **Charles B. Meding** (86), surgeon, New York, Oct. 15; **William J. Michener** (66), of Lansdowne, Pa., mechanical engineer, Philadelphia, Sept. 26; **Harold A. Miller, Sr.** (—), surgeon, Augusta, Ga., Sept. 22; **Howard U. Miller** (72), internist, Reading, Pa., Sept. 28; **Leo E. Miller** (65), of Stratford, Conn., author and explorer, New Haven, Oct. 6; **Paul A. Neal** (51), biologist, Bethesda, Md., Oct. 13; **Ferdinand Nissen** (51), economist, New Rochelle, N. Y., Oct. 15; **James H. O'Connell** (90), heating engineer, Leonia, N. J., Oct. 10; **John H. Pitman** (62), mathematician and astronomer, Swarthmore, Pa., Sept. 23; **Frederick Prime** (71), radiotherapist, New York, Oct. 13.

Donald A. Rankin (46), chemist, Edgewater, N. J., Sept. 19; **Oliver G. Ricketson** (58), of South Dartmouth, Mass., archaeologist and explorer, Bar Harbor, Me., Oct. 17; **Michael I. Rostovtzeff** (81), archaeologist, New Haven, Conn., Oct. 20; **Oscar M. Schloss** (69), pediatrician, Southold, N. Y., Oct. 13; **Sylvia B. Simon** (43), psychiatrist, New York, Oct. 8; **Frederick A. Spencer** (67), electrical engineer, Northfield, Vt., Oct. 8; **Otto Szasz** (67), of Cincinnati, mathematician, Chambey-on-Montreux, Switzerland, Sept. 19; **John W. Vollmer** (—), physician, Wilton, Conn., Oct. 16; **Arthur L. Walker** (89), metallurgist, Whippany, N. J., Sept. 30; **Joseph J. Walsh** (78), of Wilkes-Barre, mine safety engineer, Harrisburg, Pa., Sept. 20; **Edwin F. Wendt** (83), civil engineer, Pittsburgh, Pa., Sept. 30; **William L. White** (44), of Arlington, botanist, Concord, Mass., July 31; **Louis T. Wright** (61), surgeon, New York, Oct. 8.

Technical Papers

The Effect of 2-Aminofluorene on the Utilization of S^{35} DL-Methionine[1]

A. W. Wase, J. B. Allison, and J. F. Migliarese

Bureau of Biological Research, Rutgers University, New Brunswick, New Jersey

Impaired utilization of protein by rats and dogs fed 2-acetyl-aminofluorene has been demonstrated together with the protective effects of dietary riboflavin (*1–5*). Studies have been planned to determine the effects of this carcinogen on the utilization of some of the essential amino acids. The following is a preliminary report involving S^{35} DL-methionine.

The experiments involved both *in vivo* and *in vitro* studies of the uptake of S^{35} DL-methionine by the livers of rats. The *in vitro* experiments were planned as follows:

Livers from normal rats were sliced and perfused in cold Krebs saline. The slices were removed, blotted dry, and placed in a medium consisting of Krebs-buffered saline containing 30 mg% S^{35} DL-methionine with a specific activity of 167 c/m/mg DL-methionine. The system was incubated at 37° C for 2 hr in an air atmosphere.

Similar systems were employed, including 2-aminofluorene in concentrations ranging from 19.6 to 98.0 μg AF · HCl/100 ml buffered saline, with and without riboflavin in several progressive concentrations. Following the incubation period, slices were removed, washed, blotted dry, digested in HNO_3, and an aliquot was assayed for radioactivity. Results are expressed in terms of μg of methionine incorporated per gram of liver slices.

The *in vivo* experiments were carried out as follows: Two groups (12 each) of adult (200–250 g) male Wistar rats were fed the basal 18% casein diet (*4*), one group receiving .03% of the carcinogen in the diet. The animals were fed *ad lib* for a period of 56 days. At the end of this experimental period each animal was given 3 mg S^{35} DL-methionine intraperitoneally. After 24 hr, half the animals in each group were killed and the livers removed. Livers were washed in cold saline, blotted dry, and weighed. Samples of approximately ½ g were taken for radioactivity assay. After 72 hr the remaining rats were autopsied and treated as above.

Previous studies have demonstrated that aminofluorene compounds inhibit the growth and utilization of nitrogen by animals (*1–5*), an inhibition which is overcome by riboflavin. The data in Table 1 illustrate another example of inhibition by 2-aminofluorene overcome by this vitamin.

The incorporation of S^{35} DL-methionine in liver slices is decreased markedly by the presence of AF · HCl. This inhibition is reversed and the uptake returned to normal with the introduction of riboflavin into the system. It is possible that the addition of 2-aminofluorene may alter intermediary metabolic processes involving methionine, thereby depleting the animal in protein stores (a depletion), which is overcome with riboflavin. This possibility is under investigation.

Animals with depleted protein stores exhibit an increased tendency to utilize and retain dietary amino acids, an increase in protein anabolism that is associated with growth and regeneration (*6*). It is interesting to note that the amount of S^{35} DL-methionine taken up by the liver in 24 hr is greater in animals fed the carcinogen for 56 days (Table 2), although this greater uptake is followed in the next 48 hr by a more rapid loss than normal. The enzymatic significance of this greater uptake and utilization of S^{35}

TABLE 1

EFFECT OF VARYING 2-AMINOFLUORENE (AF) AND RIBOFLAVIN ON THE UPTAKE OF S^{35} DL-METHIONINE IN RAT LIVER SLICES

2-Aminofluorene (μg/ml)	Riboflavin (μg/ml)	Uptake (% of controls)
0.000	0.00	100.0
0.05	—	68.3
0.10	—	56.0
0.20	—	42.0
0.40	—	31.5
1.0	—	31.1
0.05	0.06	79.3
0.05	0.13	99.6
0.20	0.18	101.0
0.20	0.24	98.0
0.20	4.00	99.2
—	0.06	99.2
—	0.13	106.5
—	0.24	102.7
—	1.17	105.0
—	4.00	98.0

TABLE 2

UPTAKE (24 HR) AND UTILIZATION (72 HR) OF METHIONINE (CALCULATED FROM THE ACTIVITY OF S^{35}) IN LIVERS OF RATS FED DIET WITH OR WITHOUT 2-ACETYL AMINOFLUORENE FOR 56 DAYS. EACH VALUE AN AVERAGE ON 6 ANIMALS

	Methionine			
	24 hr	72 hr	24 hr	72 hr
Diet	μg/liver		μg/liver/100 g body wt	
18% Casein	142 ± 11	87 ± 9	558 ± 42	317 ± 29
18% Casein + 0.03% 2-acetyl aminofluorene	180 ± 13	78 ± 12	1165 ± 59	472 ± 33

[1] This work was supported by a grant from the American Cancer Society upon recommendation of the Committee on Growth of the National Research Council.

DL-methionine in animals treated with carcinogen is under investigation. It is thought possible that increased utilization of S^{35} DL-methionine may be associated with a greater potential for growth or regeneration of tissues, a hypothesis that is being tested in normal and protein-depleted rats.

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On the Anomaly in the Heat Capacity of Manganous Oxide[1]

Roald K. Wangsness

U. S. Naval Ordnance Laboratory, White Oak, Maryland

Recent work of Todd and Bonnickson (*1*) on very pure samples of MnO shows that as the temperature increases in the range from 100° to 122° K the heat capacity of MnO rises from about 7 cal/(mole deg) to a peak of 76.7 and then drops sharply to about 7.5. The total heat absorbed is 246 cal/mole. The average Debye heat capacity is about 7, so that $7 \times 22 = 154$ cal/mole are absorbed by lattice oscillations. One can estimate the additional heat capacity associated with the disappearance of the spontaneous magnetization to be R (*2*), so that the heat ascribable to this effect is 44 cal/mole. Thus, there is an amount of heat $q = 48$ cal/mole (nearly 20% of the total) which cannot be accounted for by the usual mechanisms.

MnO is antiferromagnetic with $\theta = -610°$ K and $T_c \simeq 122°$ K, where θ and T_c are the characteristic temperature of the Curie-Weiss law and the Curie temperature, respectively (*3*). The fact that $-\theta/T_c$ is equal to 5 rather than unity, as predicted by the simple theory, has been discussed by means of an extension of the molecular field theory to include the effects of nearest and next-nearest neighbor interactions in more complicated orderings of the elementary moments contained in the magnetic sublattices (*4*). If γ_1 and γ_2 are the molecular field coefficients for nearest and next-nearest neighbor interactions, respectively, then the ratio $-\theta/T_c$ for MnO determines $\rho = \gamma_2/\gamma_1$, to be 0.75; this value is compatible with two different orderings known as ordering of the second or third kind, which can occur if ρ is greater or less than 3/4, respectively. Neutron diffraction experiments have shown the ordering below the Curie temperature to be of the second kind (*5*).

It has been found (*6*) that the lattice constants of MnO change in this temperature range, and since γ_1 and γ_2 (and thence ρ) presumably depend strongly upon distance, it is suggested that the anomalous behavior can be further interpreted as a change from the second to the third kind of order as the temperature is increased. To correspond to the neutron diffraction results, we should have $\rho = (3/4) + \delta$ below the Curie temperature, and $\rho = (3/4) - \varepsilon$ throughout the transition region to conform to this suggestion (δ and ε are small positive numbers). The following calculations provide some quantitative support for this interpretation.

If T_i is the Curie temperature for the ith kind of ordering, one finds that

$$T_2 = C\,\rho\,\gamma_1,\ T_3 = C\,\gamma_1\,[1 - (1/3)\,\rho],$$

and

$$-\theta = 3C\,\gamma_1\,[1 + (1/3)\,\rho]$$

where C is the Curie constant (*4*). A reasonable expression for the range ΔT of the anomalous behavior is $T_3 - T_2$, so that we obtain

$$\Delta T = -(\theta/3)\left(1 - \frac{4}{3}\rho\right)\left(1 + \frac{1}{3}\rho\right)^{-1} \simeq (16/9)\,T_c\varepsilon.$$

Using the experimental values of ΔT and T_c, we find the estimated value of ε to be 0.1. This corresponds to a 13% change in ρ which is satisfactorily small considering the nature of the calculation.

The energy which must be supplied to the system when in the ith kind of ordering in order to destroy the magnetization is of the order of RT_i. Thus, for the heat absorbed during the change of ordering, we can write

$$q = R(T_3 - T_2) = (16/9)RT_c\varepsilon.$$

From this we find that $q = 43$ cal/mole, which agrees quite well with the value of 48 given above.

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Ammoniated Dentifrices and Hamster Caries: Further Studies on the Effects of Ingestion[1]

David F. Mitchell, Edith Zak Helman, and Dwight S. Chernausek

School of Dentistry, University of Minnesota, Minneapolis

Controversy exists concerning the efficacy of ammoniated dentifrices in dental caries prevention. *In*

[1] Work supported by grants-in-aid from the U. S. Public Health Service and from the Graduate School, University of Minnesota.

vitro and *in vivo* studies that give evidence of effectiveness (*1, 2*), and others that do not, have been reported (*3, 4*). A dentifrice containing dibasic ammonium phosphate (5%) and urea (3%) has been advocated. It was believed that the ammonium ion has a specific inhibitory action on the caries process and that the two aforementioned compounds act synergistically in inhibiting decay.

A previous report (*5*) has shown a reduction in caries in hamsters that ingested a caries-producing diet containing dibasic ammonium phosphate (1%) and urea (0.6%). However, it was also shown, in a toothbrushing study, that a control dentifrice was just as effective as an ammoniated dentifrice in inhibiting hamster caries (*6*).

The study reported here was designed to test the individual effectiveness of dibasic ammonium phosphate and urea, and to recheck the value of a combination of these compounds. In addition, dibasic sodium phosphate (having the same buffering capacity against acids as dibasic ammonium phosphate) was fed alone and in combination with urea to test the possible specificity of the ammonium ion.

occurring solely through chance is also tabulated. The results again show that male animals undergo a greater caries experience during the experimental procedures. In the female mean scores, dibasic ammonium phosphate (Group B) appears to be the most effective in reducing caries experience; urea (Group C) appears to be ineffective; and the combination (Group D) appears to be effective, thus corroborating results of a previous study (*5*). A similar pattern is shown in the male mean scores.

The statistical tests appear to be highly significant when testing the difference between certain means of the male grouping. A parallel relationship is also apparent in the female grouping. It appears that the ammonium ion does not play a specific role, since dibasic sodium phosphate may be substituted for dibasic ammonium phosphate and the beneficial caries-reducing effect will still be present. Urea in the concentration used (0.6%) did not seem to be effective in reducing the caries scores in the female animals; however, it appeared to be of some value in reducing the caries scores of the male animals. It should be noted that in neither case was an additive or synergistic effect apparent. It would appear that the inhibitory mechanism of the two dibasic compounds tested might result from their buffering action in maintaining an alkaline pH.

Urea may be of aid in preventing dental caries, and further experiments are being conducted to evaluate its position.

TABLE 1

CARIES SCORES (mm^2)

	No. animals	Mean ± S D	*P* values		
			A	B	C
Females					
A, control	12	500 ± 132			
B, 1% $(NH_4)_2HPO_4$	30	399 ± 122	B .02	—	—
C, 0.6% urea	12	499 ± 100	C .66	.06	—
D, 1% $(NH_4)_2HPO_4$ + 0.6% urea	25	415 ± 119	D .06	.66	.13
Males					
A, control	15	706 ± 171	B .001	—	—
B, 2.03%* $(Na)_2HPO_4 \cdot 7H_2O$	19	382 ± 118	C .04	.001	—
C, 0.6% urea	18	581 ± 160	D .001	.16	.001
D, 2.03%* $(Na)_2HPO_4 \cdot 7H_2O$ + 0.6% urea	26	429 ± 97			

* Equivalent in molar concentration to 1% $(NH_4)_2HPO_4$. The pH of the diets containing the dibasic compounds was 6.7.

After weaning at 21 days of age, 240 animals were divided into eight equal groups and fed a caries-producing diet,[2] beginning at 30 days of age, for 105 days. A sex difference in caries-susceptibility requires a control group for each sex. In the interests of economy, therefore, four groups were females, and four groups males. Table 1 indicates group distribution and drugs tested. Unfortunately, a salmonella epidemic reduced the number of survivors in most groups.

The carious lesions were outlined on charts, blackened with tempera paint, and scored by an instrument employing a photosensitive plate. The total occlusal area affected was recorded in mm^2 (*7*). The mean caries scores are listed in Table 1. Statistical tests of the difference between means were done. The probability (*P*) of such a difference between the means

[2] Whole wheat flour, 30%; whole powdered milk, 30%; cornstarch, 20%; confectioner's sugar, 15%; alfalfa meal, 4%; sodium chloride, 1%.

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Histochemical Demonstration of Aryl Sulfatase[1]

Alexander M. Rutenburg, Richard B. Cohen,[2] and Arnold M. Seligman[3]

Yamins Laboratory for Surgical Research, Beth Israel Hospital, and Department of Surgery, Harvard Medical School, Boston, Massachusetts

In a previous search for a suitable substrate to demonstrate sulfatase activity histochemically, it became apparent that enzymatic activity was sufficiently low in mammalian tissues to require hours of incubation, that the optimum pH was too low for rapid coupling with diazonium salts, and that the enzyme itself was readily diffusible. By the selection of a colorless substrate, made soluble by the sulfate group, that would yield a naphthol sufficiently insoluble in water to remain at the site of enzymatic hydrolysis, coupling to a blue azo dye was made possible at higher pH afterward (*1*). The problem was also made easier by the discovery that aryl sulfatase activity in rodents withstood fixation of tissue in cold 10% neutral formalin (*1, 2*). This was not the case with monkey and human tissues. Whereas diffusion of the enzyme produced artifacts after incubation of fresh frozen sections for more than 2 hr, similar diffusion artifacts usually did not appear until after 3 hr of incubation of formalin-fixed tissue.

Following exploration of several substituted naphthols, 6-bromo-2-naphthol provided the most satisfactory sulfate ester (*1*). However, incubation for 12–24 hr was necessary in order to produce tissue sections with enough stain (*1*). Following the synthesis of 6-benzoyl-2-naphthol (*3*), it was found that its sulfuric acid ester was hydrolyzed enzymatically only slightly faster than the bromo analog. However, the color density of the azo dye produced with tetrazotized diorthoanisidine was about twice as great per mole in the case of the benzoyl naphthol as with the bromonaphthol. This enabled shortening the incubation period to 2–4 hr with tissues of high enzymatic activity and 6–12 hr with others. With formalin-fixed tissue, diffusion of the enzyme was usually not significant in 3 hr. With tissues requiring longer incubation and with all unfixed tissues, enzyme diffusion was prevented only by increasing the salt content of the medium. This procedure has been necessary in the case of other diffusible enzymes: esterase (*4, 5*), acid phosphatase (*6*), and β-D-galactosidase (*7*). In the case of β-D-glucosidase, all attempts to control enzyme diffusion by increasing the salt content of the medium failed because of inhibition of enzymatic activity (*8*).

[1] This investigation was supported by a research grant from the National Cancer Institute, National Institutes of Health, USPHS, by an institutional grant to Harvard University from the American Cancer Society, and by the Slosberg Fund for Research in Diabetes.

[2] Research Fellow of the National Cancer Institute.

[3] Acknowledgment for technical assistance is due Virginia Rosenberg, Martin Hyman, and Elginne Johnson. Photomicrography is by Leo Goodman.

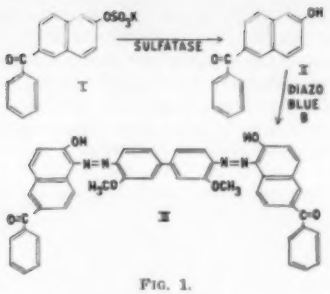


FIG. 1.

Sulfatase activity in tissue sections was slightly inhibited by 3% sodium chloride, whereas fresh tissue homogenates were not affected.

The substrate,[4] potassium 6-benzoyl-2-naphthyl sulfate (Fig. 1, I), was prepared from 6-benzoyl-2-naphthol (II) (*3*) as follows: Chlorosulfonic acid (7.5 ml) was added cautiously in small portions to anhydrous pyridine (50 ml) in an Erlenmyer flask surrounded by an ice bath. In the course of a vigorous reaction a white crystalline mass of sulfur trioxide formed. A solution of 6-benzoyl-2-naphthol (25 g) in anhydrous pyridine (50 ml) was added all at once. The mixture was stirred and heated to the boiling point, where it was held for 2–3 min. The solution was cooled and transferred to a 3-liter beaker with absolute methanol (100 ml). A saturated solution of methanolic potassium hydroxide was added in small portions until the solution was alkaline. A darkening of the solution occurred on passing the neutral point. A large excess of alkali was avoided. A white heavy precipitate separated during this procedure. Dry ether (2 liters) was added, and the salts were collected with suction, washed with

TABLE 1

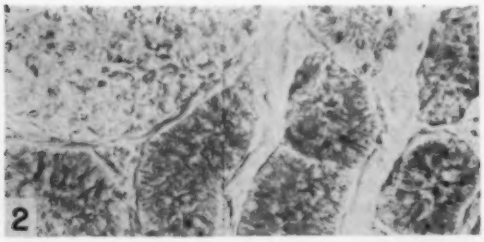
ARYL SULFATASE ACTIVITY OF ORGANS FROM 4 RATS MEASURED BY INCUBATING AQUEOUS EXTRACTS OF HOMOGENATES (10 MG) WITH POTASSIUM 6-BENZOYL-2-NAPHTHYL SULFATE FOR 4 HR AT PH 6.1 AND 37° C

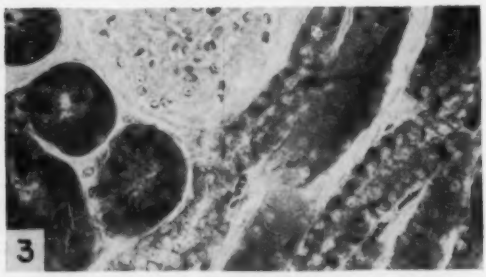
Organ	Micrograms 6-benzoyl-2-naphthol formed in 4 hr	
	Range	Average
Liver	36–64	45
Kidney	22–32	28
Pancreas	18–40	26
Adrenal	16–18	18
Testis	6–10	7
Small intestine	6–8	7
Lung	6–8	7
Large intestine	1–9	6
Brain	4–7	6
Spleen	2–10	5
Heart	4–7	5
Skeletal muscle	4	4
Salivary gland	2–6	4
Stomach	2–4	3

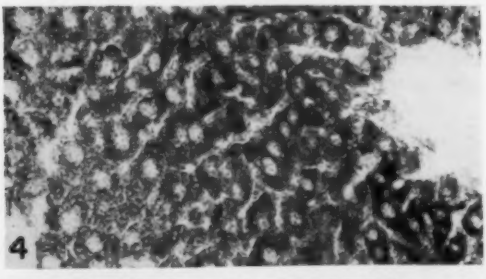
[4] The substrate and reagents may be purchased from Dajac Laboratories, Monomer-Polymer, Inc., 511 Lancaster St., Leominster, Mass.

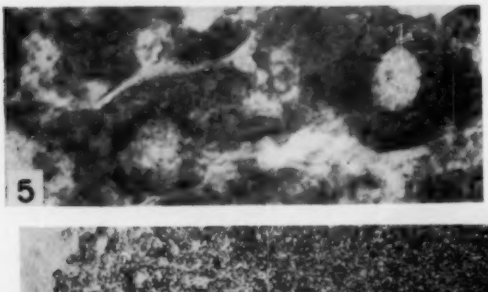
ether, and dried. The white powder was suspended in 100 ml of cold distilled water for 30 min in order to remove potassium chloride and potassium sulfate (inhibits aryl sulfatase). The poorly soluble potassium 6-benzoyl-2-naphthyl sulfate was collected with suction, washed with a little cold water, acetone, and ether, and dried; yield 26 g (74%).

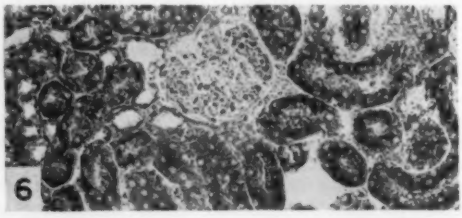
By means of a calibration curve prepared with 6-benzoyl-2-naphthol and tetrazotized diorthoanisidine (Diazo Blue B) in the presence of tissue protein, aryl sulfatase activity was determined colorimetrically in extracts of fresh tissue homogenates. Although details of the procedure will be published elsewhere, enzymatic activity of several organs of the rat is given in

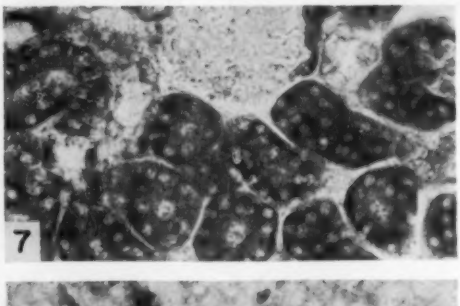


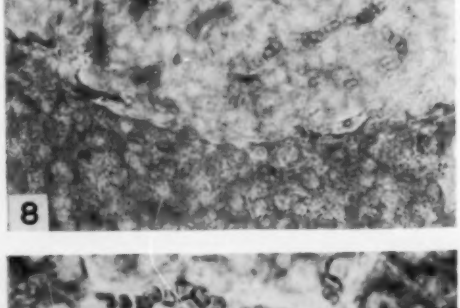












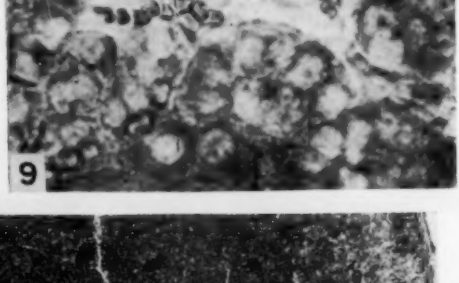


Table 1. The highest activity was found in liver, kidney, pancreas, and adrenal gland.

Phenol sulfatase demonstrated colorimetrically with potassium *p*-nitro phenyl sulfate has been reported highest in liver, adrenal gland, and kidney of the rat (*9*). Phenol sulfatase demonstrated gravimetrically with potassium phenyl sulfate was found in liver, kidney, muscle, and brain of rabbits (*10, 11*); kidney, brain, liver, duodenum, spleen, lung, muscle, small intestine, and pancreas of man (*12*); and kidney and brain of pig, calf, and rabbit (*13*).

For the histochemical procedure, tissues were obtained from freshly exsanguinated animals, at operation, or at autopsy on man. It was found that animal tissues could be stored at 4° C for 24–48 hr without serious loss of enyzmatic activity. The tissues of rat, mouse, and hamster withstood fixation in cold, neutral, 10% formalin for as long as 120 days with some loss (10–50%) in enzymatic activity. In the monkey and man, however, sulfatase activity of liver, kidney, and pancreas was nearly completely destroyed by cold formalin within 24 hr. Prior exposure of liver and kidney of the mouse and rat to other fixatives at 4° C for 4 hr resulted in loss of enzymatic activity as follows: acetone or absolute ethanol, 20–40%; ethylene glycol dimethyl ether, 60–80%; and absolute methanol, 90–100%.

After fixation in formalin the blocks of tissue (3–5 mm thick) were washed twice in 0.85% sodium chloride solution for 30 min, and frozen sections (15–20 μ) were cut with a freezing microtome, and 8–10 sections were transferred directly from the knife and floated on 10 ml of the substrate solution. They were then transferred to 20 ml of the substrate solution in a beaker for incubation. Tissues from monkey and man were not fixed, and frozen sections (10–20 μ) were cut according to the Coons' modification of the Linderström-Lange technique (*14*), mounted on glass slides, and air-dried. The slides were then incubated in the substrate solution made hypertonic according to the procedure given below. The enzymatic reaction was somewhat slower in sections which were mounted on glass slides and air-dried.

The substrate solution was prepared by dissolving potassium 6-benzoyl-2-naphthyl sulfate (25 mg) in hot, 0.85% sodium chloride solution (80 ml) and adding 0.5 *M* acetate buffer, pH 6.1 (20 ml). The solution was stable and could be stored at room temperature for at least 15 days. Substrate solution was made hypertonic by the addition of solid sodium chloride (2.6 g) to each 100 ml of substrate solution. To prevent extensive histologic distortion, the sections were immersed briefly (2–5 min) in three solutions of sodium chloride (0.85%, 1%, and 2%) prior to incubation in the hypertonic substrate solution (*7*).

Tissues with greater enzymatic activity were incubated at 37° for 2–3 hr in the substrate solution, and tissues with low activity were incubated for 4–16 hr in the hypertonic substrate solution. All fresh frozen sections were also incubated in the hypertonic substrate solution. Sections from each organ were incubated in separate containers.

Following incubation the sections were washed twice (10–15 min each) in cold saline (fresh tissue) or water (formalin-fixed tissue). Sections that had been incubated in hypertonic substrate solution were returned to 0.85% sodium chloride solution after prior immersion in graded concentrations of the salt. After washing, the sections were transferred to a cold (4° C), freshly prepared solution of tetrazotized diorthoanisidine (1 mg/ml) in 0.05 *M* phosphate buffer, pH 7.6. The sections were gently agitated for 5 min. They were washed 3 times in cold 0.85% sodium chloride solution and water (15 min each) and mounted on a glass slide with glycerine or glycerogel. The cover slip was sealed with fingernail polish.

Coupling of 2 molecules of 6-benzoyl-2-naphthol with the tetrazonium compound yielded a deep blue dye (Fig. 1, III), whereas monocoupling produced a red dye. However, solutions of the blue dye in many organic solvents and in lipoid were red by transmitted light. The intensity of the pigment, as well as the color, was related to the degree of enzymatic activity. Tissues with high sulfatase activity stained blue, and those with low activity stained red or purple. The blue dye was stable in these sections for only about 15 days at 4° C. Thereafter, the blue pigment changed to purple and finally red, and the localization of the dye became fuzzy. This process was accelerated when sections were

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FIGS. 2–10: FIG. 2. Dog kidney fixed in formalin for 24 hr. Sulfatase activity is absent. Incubation period, 24 hr; no filter. ×350.

FIG. 3. Dog kidney fixed in formalin for 24 hr (adjacent section to Fig. 2). Incubated 24 hr together with sections of fresh rat kidney. Sulfatase activity is present in the section of dog kidney (*cf.* Fig. 2). Staining is confined to the cytoplasm of tubular epithelium, presumably as a result of diffusion of the enzyme from the sections of rat kidney. Green filter. ×350.

FIG. 4. Mouse liver fixed in formalin for 24 hr. Incubated 4 hr. Enzymatic activity is highest (blue) in the periportal area (right) and is lower in the surrounding region (red). Hepatic cell nuclei, walls of blood vessels, and erythrocytes are free of sulfatase. Green filter. ×375.

FIG. 5. Rat liver fixed in formalin for 24 hr. Incubated 4 hr. Cytoplasm localization of the enzyme is shown. Green filter. ×950.

FIG. 6. Mouse kidney fixed in formalin for 24 hr. Incubated for 8 hr in hypertonic substrate solution. Cytoplasm of tubular epithelium has sulfatase activity. Cell nuclei, glomeruli, and blood cells in the glomeruli are unstained. Green filter. ×350.

FIG. 7. Rat kidney fixed in formalin for 24 hr. Incubated for 4 hr. Same localization of sulfatase as Fig. 6. Green filter. ×375.

FIG. 8. Rat pancreas fixed in formalin for 48 hr. Incubated in hypertonic substrate for 12 hr. Islet of Langerhans (top) has much less sulfatase activity than acinar cells. Erythrocytes in capillaries of the islet are unstained. Green filter. ×400.

FIG. 9. Unfixed human pancreas (surgical biopsy). Incubated in hypertonic substrate for 4 hr. Cytoplasmic localization of sulfatase activity is shown. Green filter. ×850.

FIG. 10. Rat adrenal gland fixed in formalin for 96 hr. Incubated for 4 hr. All zones of the adrenal cortex are stained. The adrenal medulla (left) and transitional zone (right) show very little sulfatase activity. Erythrocytes are unstained. Green filter. ×150.

stored at room temperature (2 days) or exposed to heat (minutes). The sections were redder with tissues containing much lipoid. The use of higher than recommended concentrations of the tetrazonium compound or coupling above 4° C resulted in the formation of more of the red than of the blue pigment.

Diffusion of the enzyme was carefully checked in every batch of sections by testing for the naphthol in the supernatant incubation medium. In order to do this the pH was elevated to 7.4 to 7.6 with solid sodium bicarbonate, and tetrazotized diorthoanisidine was added. Significant diffusion was shown by production of the azo dye. Under conditions that prevented diffusion of the enzyme, or when the incubation period was sufficiently short, only a slight pink coloration was produced in the supernatant; otherwise the color was deep red to blue. The importance of diffusion of the enzyme was shown in experiments in which frozen sections of fresh or formalin-fixed dog kidney, which normally do not have sulfatase activity (Fig. 2), were incubated in the same flask (10 ml) with an equal number of fresh frozen sections of rat kidney for 4–24 hr. The sections of dog kidney were intensely stained (Fig. 3), and the pattern of distribution was similar to that of rat kidney. When the sections of fresh dog kidney were incubated separately in an aqueous extract of homogenized rat liver or kidney for 4 hr at 37° and rinsed briefly, subsequent incubation in substrate medium for 4 hr gave a similar distribution, but paler and less distinct stain in the dog kidney. Longer washing prior to incubation in the substrate, or the use of formalin-fixed sections of dog kidney, resulted in even less staining. These experiments indicated that diffusion of the enzyme rather than diffusion of naphthol was largely responsible for the phenomenon.

That diffusion of the naphthol from sections was not significant was shown in other experiments in which 8–10 sections containing the naphthol released by enzymatic hydrolysis intracellularly were suspended in 20 ml of wash fluid and gently agitated for 30–40 min. Naphthol could not be demonstrated in the wash fluid. Furthermore, it was shown that movement of naphthol from the supernatant fluid into the section was not likely to produce serious artifacts, since formalin-fixed sections, incubated for 4 hr at 37° C in a saturated aqueous solution of 6-benzoyl-2-naphthol, and subsequently washed and coupled with the tetrazonium compound, showed only a diffuse, indistinct, pale-purple stain in the cytoplasm of epithelial cells. Longer incubation or incubation in 15% ethanol solution containing more of the naphthol (40 μg per ml) produced more intensely, but diffusely and irregularly stained, sections. Fresh frozen sections were stained more intensely than formalin-fixed sections. The naphthol could be extensively removed by washing them prior to coupling, but it was less readily removed if it had been liberated intracellularly by enzymatic hydrolysis. This suggests that the naphthol in the diffusion experiments may be attached to different portions of the cell; hence it was necessary to take the precautions described above in order to avoid artifacts caused by diffusion of enzyme and naphthol.

The four organs (rat) found to have high enzymatic activity by colorimetric determination (Table 1) were studied histochemically in the mouse, rat, hamster, guinea pig, rabbit, dog, rhesus monkey, and man. The intensity of staining of each organ varied among individuals of each species and particularly from one species to the next, but the pattern of distribution for each organ was similar in all species. In general, enzymatic activity was present in the cytoplasm of epithelial cells and was absent from cell nuclei, smooth muscle, and connective tissue. Although elastic tissue of some blood vessels (human pancreas) was well stained, this presumably was not due to enzymatic hydrolysis, because other naphthols, particularly those with electron-attracting groups which enhance the acidity of the hydroxyl group, have shown an affinity for elastic tissue (*15*).

The kidney and liver of the mouse, rat, monkey, and man, and the kidney, but not the liver, of the hamster stained intensely. These organs showed very little activity in the guinea pig, rabbit, and dog. A high order of activity was noted in the pancreas of the rat, hamster, monkey, and man, but not in the mouse, guinea pig, rabbit, and dog. The adrenal gland of the rat and hamster stained less intensely than the corresponding kidney and pancreas. Mouse adrenals showed even less activity than in the rat and hamster, and very little activity was seen in the adrenals of guinea pig, rabbit, dog, monkey, and man. Organs with a very low order of sulfatase activity showed a diffuse, light-purple stain after long incubation (16–24 hr). Localization of the enzyme was unsatisfactory in these sections because of enzyme diffusion and lipoid solubility of the azo dye.

The cytoplasm of epithelial cells of the liver (Fig. 5) was stained a diffuse blue to purple color. More activity was noted in the hepatic cells of the periportal (Fig. 4) and pericentral regions of the liver lobule. In the intermediate areas the cells were red and purple.

In the kidney cortex (Figs. 6, 7) the cytoplasm of the epithelial cells of all parts of the nephron except the glomerulus was stained intensely blue or purple. The glomerulus and blood cells in the capillaries of the glomerulus were unstained. The proximal and distal convoluted tubules were darker than other parts of the nephron. Collecting tubules and other elements of the medulla were not stained.

In the pancreas (Figs. 8, 9) the cytoplasm of acinar cells was stained purple, and the pigment was concentrated in the perinuclear reigon. In a few acini, staining was most marked in the basilar portion of the cells. The islets of Langerhans stood out from the surrounding acinar cells because of their much paler stain (Fig. 8). Epithelial cells of the ducts were also less intensely colored than the acinar cells, and the pigment was confined to the apical portion of these cells.

Sulfatase activity was present in all parts of the adrenal cortex (Fig. 10). Color was most intense in the zona fasciculata and least in the transitional zone.

Cytoplasmic staining was homogeneous except in the zona reticularis, where red and purple droplets stood out against the red cytoplasmic background, perhaps because of solution of the dye in fat droplets. Cell nuclei and the capsule of the gland were unstained, and cells of the adrenal medulla stained very lightly.

Sulfatase activity was not demonstrable in rat and mouse collagen, cartilage, bone, and blood cells.

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The Destruction of Epinephrine by the DOPA-Oxidase System of Ocular Tissue[1]

Winifred J. Angenent and George B. Koelle[2]

Department of Pharmacology,
College of Physicians and Surgeons,
Columbia University, New York City

The principal enzyme systems responsible for the inactivation of epinephrine in the body are generally considered to be monoamine oxidase and cytochrome oxidase (*1–3*); in addition, epinephrine is conjugated in the liver. In seeking a possible enzymatic basis for the observation that mydriatics are more effective in light than in dark eyes (*4*), assays were conducted on homogenates of the irides and ciliary bodies of pigmented and albino rabbits for enzymes which might be involved in the destruction of the cholinergic or adrenergic mediators. No significant differences were found between the two groups in respect to monoamine oxidase (*5*), cytochrome oxidase, succinic dehydrogenase (*6*), cholinesterase (*7*), or reducing substances (*8*), employing the specific substrates called for by the methods listed. Dihydroxyphenylalanine (DOPA) was oxidized by the pigmented but not by the albino homogenates; DOPA-oxidase has previously been demonstrated in the pigment granules of steer irides (*9*). It appeared that this enzyme was responsible for the small but consistent difference in O_2-uptake observed when epinephrine was used as substrate, since preparations of melanomas have been reported to oxidize epinephrine, although at rates considerably below those for DOPA (*10, 11*). When a mixture of epinephrine plus DOPA was used as substrate, the O_2-uptake by the pigmented homogenates was considerably greater than the sum of the values with the two substances alone (Fig. 1). When the concentrations of the two substrates were varied, the rate was found to be dependent upon the concentration of each. Bio-assays of trichloracetic acid filtrates of the reaction mixtures by the dog's blood pressure method showed that significant amounts of epinephrine were inactivated during the reaction. A lower degree of augmentation of O_2-uptake was recorded with the vessels in which autoxidation was followed, but none occurred with the albino homogenates. Recent evidence has indicated that mammalian "DOPA-oxidase" and "tyrosinase" are identical (*12*). The addition of 0.001 *M* α-naphthothiourea (ANTU), a relatively selective inhibitor of plant tyrosinase (*13*), reduced the O_2-uptake by 50% during the first hour in vessels containing the combined substrate and pigmented homogenate, but did not affect the rate of autoxidation. No significant degree of deamination or decarboxylation occurred during the enzymatic or spontaneous oxidation. When mixtures of DOPA and norepinephrine were used as substrate, the augmentation of O_2-uptake was absent.

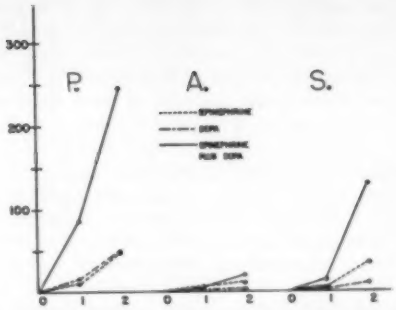

Fig. 1. Rates of oxygen uptake of homogenates of pigmented (*P.*) and albino (*A.*) rabbit iris-ciliary bodies, and spontaneous oxygen uptake (*S.*), in the presence of epinephrine (2.75 mg), D-L-DOPA (2.0 mg), and epinephrine plus DOPA. Each flask contained 60–75 mg wet wt tissue in 0.133 *M* phosphate buffer (pH 7.0), 38° C, total fluid volume 3.0 ml. Points represent averages of two to four determinations. Ordinates: μl O_2/100 mg wet wt tissue; abscissae: time in hours.

The development of a reddish-orange color prior to a fine black precipitation in the autoxidation vessels and in the supernatant solutions with pigmented homogenates, and the absence of deamination or decarboxylation, indicate that both substrates followed the same path of oxidation to and beyond indole-quinones as they have been shown to follow with plant tyrosinase (*14, 15*). The basis of the greatly augmented O_2-uptake with the combined substrates remains to be determined. The quinone and indole-quinone forms of epinephrine and DOPA constitute redox systems; the

[1] This investigation was supported by a research grant from the National Institutes of Health, USPHS.

[2] We wish to thank DeWitt Smith and Gilbert Mudge and his staff for generous help in obtaining fresh rabbit eyes.

quinone forms are highly unstable (*16*). It is possible that the oxidant of one form of either compound may promote directly the oxidation of some stage of the other. Another possibility is that liberation of hydrogen peroxide with the oxidation of the leuko-form of either indole-quinone may oxidize either or both substrates (*15*). The absence of acceleration with norepinephrine is in keeping with this concept, since it is known to be oxidized to an indole-quinone with much less ease than epinephrine (*17*). Martin *et al.* (*18*) have reported that DOPA and several phenolic compounds accelerate the destruction of epinephrine by mushroom tyrosinase, and Lerner *et al.* (*19*) have more recently found a similar accelerating action of DOPA on the oxidation of epinephrine and similar compounds by a tyrosinase prepared from mouse melanoma.

Experiments are now in progress to determine the extent to which the DOPA-DOPA-oxidase system may participate in the destruction of epinephrine in pigmented irides *in vivo*. The results of these studies and a detailed account of the present findings will be reported elsewhere.

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The Effect of Ultraviolet Radiation on Sulfhydryl and Disulfide Containing Amino Acids

Klaus Schocken

Army Medical Research Laboratory, Fort Knox, Kentucky

In previous studies quantitative measurements were made on the influence of ultraviolet irradiation on the rate of hydroxylation and of destruction of those amino acids that have been implicated in the process of skin pigmentation and erythema production (*1*). It was found that these effects were inhibited by the presence of sulfhydryl containing amino acids. The results obtained were compatible with the hypothesis of Rothman and his associates that pigmentogenic stimuli such as ultraviolet radiation cause pigmentation by oxidizing or destroying inhibitory sulfhydryl compounds, thus enabling an enzyme to act on the pigment precursor (*2*).

It thus became of interest to study the effect of ultraviolet irradiation on the possible reduction of the disulfide (—S—S—) linkage of cystine and homocystine to —SH and possible oxidation of the sulfhydryl (—SH) group of cysteine to —S—S—. Methionine was also studied.

Solutions of either cystine or cysteine in 0.1 *N* HCl and of methionine in 0.3 *N* HCl were irradiated in test tubes 1 in. in diameter mounted in running water. The height of the solutions in the test tubes varied between 0.5 and 2.5 cm. The unfiltered radiation of a Hanovia quartz mercury lamp was incident from above at 3 cm distance without any absorber (except air) between the lamp and the solution. After 30 min to 2 hr of irradiation the respective amino acid solutions were analyzed colorimetrically for cysteine and cystine (*3*) or methionine (*4*) with a recording spectrophotometer.

For irradiations with approximately monochromatic radiation, the Double Monochromator Model 300 DUV of the Farrand Optical Company was used in conjunction with the 1000-w type A-H6 G-E mercury lamp. In this case, the solutions were contained in a quartz vessel with a cross-section area of 1 cm^2. The energy measurements, made with a calibrated thermopile, were accurate within ±1%. The total energy incident on the solution was absorbed, except for small reflection losses amounting to about 4%. The reflection losses, which occur on the interfaces of the quartz cell, were not subtracted from the energies as they were measured.

In those experiments in which the isolation of homocysteine was attempted, solutions of homocystine and methionine in 0.1 *N* HCl were irradiated with the Hanovia lamp, as described above, in layers of 4 cm for 2½ hr. The procedure used in the identification of homocysteine from homocystine was as follows: The dry residues of 4 irradiations of 400 mg homocystine each in 200 ml of 0.1 *N* HCl were dissolved in 12 ml water, filtered, and neutralized with NaOH. A precipitate (I) formed at pH 5–6, which was filtered, washed with water, and then dissolved in 1 *N* HCl and reprecipitated by neutralization with NH_4OH. This procedure was repeated twice. Then the precipitate was filtered, washed with water, and dried in the desiccator *in vacuo*. To the filtrate of precipitate I, 600 mg NaOH was added, followed by 0.5 ml benzylchloride, and the mixture was shaken for 100 min in a small separatory funnel. The solution was extracted with 5 ml ether four times to remove the uncombined benzylchloride. The alkaline solution was freed from ether *in vacuo* and filtered; acetic acid was added until

TABLE 1

EFFECT OF ULTRAVIOLET RADIATION ON CYSTINE AND CYSTEINE*
(1 mg in 1.5 ml 0.1 *N* HCl)

I	II	III	IV	V	VI	VII
Amino acid irradiated (1 mg)	Time of irradiation (min)	Cystine and cysteine after irradiation (mg)	Cysteine after irradiation (mg)	Cystine after irradiation calculated by difference of columns III and IV	Amount destroyed (mg)	Degree of decomposition (%)
Cystine	30	0.821 ± 0.044†	0.283	0.538	0.179	17.9
"	60	0.702 ± 0.039	0.396	0.306	0.298	29.8
"	120	0.587 ± 0.043	0.449	0.138	0.413	41.3
Cysteine	30	1.090 ± 0.012	0.740	0.350	0	0
"	60	0.890 ± 0.047	0.591	0.299	0.110	11.0
"	120	0.560 ± 0.045	0.469	0.091	0.440	44.0

* Each value is an average of five experiments made simultaneously.
† 95% fiducial limits for the mean of cystine and cysteine after irradiation.

the solution was slightly acid to litmus. After standing 48 hr in the refrigerator at 2° C the precipitate was filtered off, washed with ice-cold water, and recrystallized from boiling water. This procedure was repeated twice. Altogether 39.9 mg of a benzylated product was obtained.

The procedure used in the attempts to identify the irradiation product of methionine was in principle the same.

The results obtained on irradiation of cystine and cysteine with the Hanovia lamp are illustrated in Table 1. It can be seen that, with increasing exposures of cystine, increasing amounts of this substance were reduced to cysteine, and simultaneously increasing amounts of it were destroyed. On irradiation of cysteine, at first only oxidation to cystine took place without destruction; then, with increasing time of irradiation, increasing destruction occurred. During the irradiations the formation of hydrogen sulfide was noticeable by odor.

It is possible that in addition to the direct effect of the ultraviolet radiation some of the oxidation effects may also have been due to the diffusion into the solution of ozone generated in the vicinity of the solutions, and to the formation of H_2O_2 in the solution.

Monochromatic irradiation (wavelength 225 mμ, spectral band width 10 mμ) of cystine (1 mg in 1.5 ml 0.1 *N* HCl) for 8 hr was found to result in approximately 16% reduction of S—S to SH in the range of energies from 0.33 to 2.50 J/mg. Similar experiments carried out with cysteine indicated a small but definite degree of oxidation of cysteine to cystine in the range of energies from 0.63 to 5.28 J/mg. No destruction of either cysteine or cystine could be detected, probably because the radiant energy was considerably less than that produced by the Hanovia lamp. The absorption of cysteine, cystine, and methionine increases with decreasing wavelength; the A-H6 mercury lamp possesses no measurable output below 225 mμ; it was established that 98% of the incident radiation was absorbed by the methionine solution, 97% by the cystine solution, and 78% by the cysteine solution at this wavelength.

After irradiation of homocystine a positive test for sulfhydryl (—SH) was obtained. From the irradiation mixture *S*-benzylhomocysteine could be isolated. The mixed melting point with an authentic sample of *S*-benzylhomocysteine gave no depression.

$C_{11}H_{15}NO_2S$. Calcd: C 58.64, H 6.71, N 6.22, S 14.23
Found:[1] C 57.95, H 7.00, N 6.78, S 13.35
C 58.31, H 7.04, N 6.58, S 13.56

Although the sulfur content is too low and the nitrogen content too high to furnish unequivocal proof of the identity, there seems little doubt that the substance is *S*-benzylhomocysteine.

The finding of the conversion of homocystine to homocysteine agrees with the observation that cystine is reduced to cysteine by ultraviolet irradiation (*5*). The precipitate I was identified as unchanged homocystine.

TABLE 2

EFFECT OF ULTRAVIOLET RADIATION ON METHIONINE*
(1 mg in 1 ml 0.3 *N* HCl)

Time of irradiation (min)	Degree of decomposition (%)
30	30.0
60	40.5
120	76.0

* Each value is an average of two experiments made simultaneously.

The results obtained on irradiation of methionine with the Hanovia lamp are illustrated in Table 2. The destruction increased with the incident energy.

Monochromatic irradiation (wavelength 225 mμ, spectral band width 10 mμ) of methionine (1 mg in 1 ml 0.3 *N* HCl) for 8 hr was found to result in approximately 10% destruction within the range of energies from 0.42 to 1.12 J.

It was found that a solution of methionine gave a

[1] The analyses were performed by Carl Tiedcke, of the Laboratory of Microchemistry, Teaneck, N. J.

positive color reaction with sodium nitroferricyanide after irradiation for 1 hr with the Hanovia lamp but not before, and not if the radiation was first passed through an acetone filter which absorbs wavelengths shorter than 300 mμ. Because of this finding the isolation of homocysteine was attempted from an irradiated methionine solution. No *S*-benzylhomocysteine could be isolated; only unchanged methionine could be identified. It is possible that methyl mercaptan CH_3SH was formed.

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Comments and Communications

Zoological Nomenclature

As from March 1, 1953, the International Commission on Zoological Nomenclature will start to vote on the following cases involving the possible use of its plenary powers for the purposes specified in brackets against each entry. Full particulars of these cases were published on August 29, 1952, in the *Bulletin of Zoological Nomenclature,* those relating to cases (1) to (4) in Part 10, and those relating to cases (5) to (14) in Part 11 of Vol. 6. (1) *Sphinx* Linnaeus, 1758 (Class Insecta, Order Peidoptera) [designation of type species]; (2) Houttuyn (M. H.), 1787, *Animalium Musei Houttuinensi Index* [suppression]; (3) *Phalaena* Linnaeus, 1758 (Cl. Insecta, Ord. Lepidoptera) [suppression, and validation as of generic status of eight terms used by Linnaeus for groups thereof: *Bombyx, Noctua, Geometra, Tortrix, Pyralis, Tinea, Alucita,* as from 1758, *Attacus,* as from 1767; and names of families based thereon; alternatively, for *Bombyx* and *Pyralis* (as from Fabricius, 1775), designation of type species]; (4) *Episema* Ochsenheimer, 1816 (Cl. Insecta, Ord. Lepidoptera) [designation of type species, thereby also preserving *Diloba* Boisduval, 1840]; (5) *cydippe* Linnaeus, 1761, *Papilio,* and *adippe* Linnaeus, 1767, *Papilio* (Cl. Insecta, Ord. Lepidoptera) [suppression, and validation of *adippe* Denis & Schiffermüller, 1775, *Papilio*]; (6) *hispidus* Olivier, 1811, *Palaemon* (Cl. Crustacea, Ord. Decapoda) [validation]; (7) *Sicyonia* Milne Edwards, 1830 (Cl. Crustacea, Ord. Decapoda) [validation]; (8) *Hymenocera* Latreille, 1819 (Cl. Crustacea, Order Decapoda) [designation of type species]; (9) *Pyramidella* Lamarck, 1799 (Cl. Gastropoda, Subclass Prosobranchia) [validation, by suppression of *Plotia* Roeding, 1798]; (10) *Dasypeltis* Wagler, 1930 (Cl. Reptilia) [validation]; (11) *Trichopsylla* Kolenati, 1863 (Cl. Insecta, Ord. Siphonaptera) [suppression]; (12) *pungens* Walcknaer, 1802, *Pulex,* and *vespertilionis* Duges, 1832, *Pulex* (Cl. Insecta, Ord. Siphonaptera) [suppression]; (13) *simus* Linnaeus, 1767, *Coluber* (Cl. Reptilia) [determination of application]; (14) *Mellita* Agassiz, 1841 (Cl. Echinoidea) [validation].

Comments on the above cases should be sent to me as soon as possible.

Francis Hemming, *Secretary*
International Commission on Zoological Nomenclature
28 Park Village East, Regent's Park
London, N.W. 1, England

Comparative Anatomy, Embryology, and Histology Synthesized

Comparative anatomy, embryology, and histology of vertebrates are usually separate semester courses in undergraduate schools—an arrangement that results in some duplication of material. For the past four years I have offered at Lawrence College a year course in vertebrate morphology, which attempts to combine the three courses into an integrated whole. After a preliminary study of testis and ovary histology and germ-cell formation, we investigate fertilization, cleavage, and germ-layer formation. Then the various body systems are studied in the following order: skeletal, muscular, nervous, endodermal, urinogenital, and circulatory. For each system the development and the microscopic and gross structure of adult morphology are considered comparatively.

The forms used are frog, chick, and pig embryos; shark, *Necturus,* alligator, and cat adults; and histological sections from the four adult forms. The approach varies with the system. In the skeletal and muscular systems, a brief histological and embryological survey is followed by much more extensive work on comparative anatomy. The embryology of the nervous system is given a great deal of time, with histology and anatomy somewhat less. The endodermal systems emphasize histology most, embryology next, and anatomy less. The embryology and histology of the urinogenital systems are considered together, with anatomy following. In the circulatory system a short study of histology is followed by study of the morphology in the frog embryo, shark, and *Necturus* adults, chick embryo, alligator adult, pig embryo, and cat adult.

Attempts are consistently made to see the finished structure of a system as a result of its ontogenetic and phylogenetic development, and the relation of its gross and microscopic structure to its physiological actions. Such a course presents a more unified and complete grasp of vertebrate morphology than the separate semester courses; it provides a good foundation for an understanding of vertebrate physiology; and it solves many problems of scheduling unevenly prepared students, with repetition of material.

The prerequisite for the course is a year of general biology or general zoology. Nine hours a week for the school year are allotted. Lectures and discussions are not at any set time but come at the beginning and end of each piece of work. On the average between seven and eight of the nine hours are spent in the laboratory.

Although several comparative anatomy teachers predicted difficulty in persuading medical schools to accept such a course, the medical schools consulted were unanimous in their approval, and some were especially encouraging. It is my opinion that the students come away with as much information as before, better and more quickly assimilated because of better understanding of relationships, and therefore more thoroughly retained. The students themselves report the course stimulating and rewarding, involving a great deal of hard work and much satisfaction during and after. Alumni who have gone on to medical school say it has been very helpful and has given them some advantages over those who had separate courses.

There is still much to be done in improving the selection and integration of material and in developing teaching aids. This work is in progress. I recommend the synthesis to the consideration of college biology departments.

RELIS B. BROWN

Department of Biology
Lawrence College

Passport Procedures

THE Department of State today (Sept. 2, 1952) made public certain new regulations pertaining to the issuance of United States passports. The regulations cover those cases which involve questions of possible subversive activities on the part of the applicant.

These regulations are designed (1) to provide for more formalized procedures within the Passport Division in cases where there is a question as to whether or not an applicant's request for a passport should be granted, and (2) to provide an applicant whose request for a passport is denied with the opportunity to appeal the adverse decision before a newly created Passport Appeals Board. At the same time, the revised regulations specify standards under which the decision to deny an application for a passport will be made.

Under the revised procedures, when derogatory information exists which, unless clarified, would result in the denial of a passport, an applicant will be notified of this fact in writing. He will also be notified:

of the reasons, as specifically as security regulations permit, upon which the tentative decision to deny the passport has been made;

of his right to discuss his application in a hearing with the Passport Division;

of his right to be represented by Counsel at this hearing, and to present additional evidence.

If the decision is unfavorable, the unsuccessful applicant will be notified of his right to appeal to the Passport Appeals Board, whose membership will include at least three Department officers who have not been previously concerned with the case.

Text of the new regulations follows:

CODE OF FEDERAL REGULATIONS
TITLE 22—FOREIGN RELATIONS

Chapter I—Department of State
Part 51—Passports

Subpart B—Regulations of the Secretary of State

Pursuant to the authority vested in me by paragraph 126 of Executive Order No. 7856, issued on March 31, 1938 (3 F.R. 681; 22 CFR 51.77), under authority of section 1 of the Act of Congress approved July 3, 1926 (44 Stat. 887; 22 USC 211 (a)), the regulations issued on March 31, 1938 (Department Order 749) as amended (22 CFR 51.101 to 51.134) are hereby further amended by the addition of new sections 51.135 to 51.143 as follows:

51.135 *Limitation on Issuance of Passports to Persons Supporting Communist Movement.* In order to promote the national interest by assuring that persons who support the world Communist movement of which the Communist Party is an integral unit may not, through use of United States passports, further the purposes of that movement, no passport, except one limited for direct and immediate return to the United States, shall be issued to:

(*a*) Persons who are members of the Communist Party or who have recently terminated such membership under such circumstances as to warrant the conclusion—not otherwise rebutted by the evidence—that they continue to act in furtherance of the interests and under the discipline of the Communist Party.

(*b*) Persons, regardless of the formal state of their affiliation with the Communist Party, who engage in activities which support the Communist movement under such circumstances as to warrant the conclusion—not otherwise rebutted by the evidence—that they have engaged in such activities as a result of direction, domination, or control exercised over them by the Communist movement.

(*c*) Persons, regardless of the formal state of their affiliation with the Communist Party, as to whom there is reason to believe, on the balance of all the evidence, that they are going abroad to engage in activities which will advance the Communist movement for the purpose, knowingly and willfully of advancing that movement.

51.136 *Limitations on Issuance of Passports to Persons Likely to Violate Laws of the United States.* In order to promote the national interest by assuring that the conduct of foreign relations shall be free from unlawful interference, no passport, except one limited for direct and immediate return to the United States, shall be issued to persons as to whom there is reason to believe, on the balance of all the evidence, that they are going abroad to engage in activities while abroad which would violate the laws of the United States, or which if carried on in

the United States would violate such laws designed to protect the security of the United States.

51.137 *Notification to Person Whose Passport Application Is Tentatively Disapproved.* A person whose passport application is tentatively disapproved under the provisions of ¶ 51.135 or ¶ 51.136 will be notified in writing of the tentative refusal, and of the reasons on which it is based, as specifically as in the judgment of the Department of State security considerations permit. He shall be entitled, upon request, and before such refusal becomes final, to present his case and all relevant information informally to the Passport Division. He shall be entitled to appear in person before a hearing officer of the Passport Division, and to be represented by counsel. He will, upon request, confirm his oral statements in an affidavit for the record. After the applicant has presented his case, the Passport Division will review the record, and after consultation with other interested offices, advise the applicant of the decision. If the decision is adverse, such advice will be in writing and shall state the reasons on which the decision is based as specifically as within the judgment of the Department of State security limitations permit. Such advice shall also inform the applicant of his right to appeal under ¶ 51.138.

51.138 *Appeal by Passport Applicant.* In the event of a decision adverse to the applicant, he shall be entitled to appeal his case to the Board of Passport Appeals provided for in ¶ 51.139.

51.139 *Creation and Functions of Board of Passport Appeals.* There is hereby established within the Department of State a Board of Passport Appeals, hereinafter referred to as the Board, composed of not less than three officers of the Department to be designated by the Secretary of State. The Board shall act on all appeals under ¶ 51.138. The Board shall adopt and make public its own rules of procedures, to be approved by the Secretary, which shall provide that its duties in any case may be performed by a panel of not less than three members acting by majority determination. The rules shall accord applicant the right to a hearing and to be represented by counsel, and shall accord applicant and each witness the right to inspect the transcript of his own testimony.

51.140 *Duty of Board to Advise Secretary of State on Action for Disposition of Appealed Cases.* It shall be the duty of the Board, on all the evidence, to advise the Secretary of the action it finds necessary and proper to the disposition of cases appealed to it, and to this end the Board may first call for clarification of the record, further investigation, or other action consistent with its duties.

51.141 *Bases for Findings of Fact by Board.* (*a*) In making or reviewing findings of fact, the Board, and all others with responsibility for so doing under ¶ 51.135–51.143, shall be convinced by a preponderance of the evidence, as would a trial court in a civil case.

(*b*) Consistent and prolonged adherence to the Communist Party line on a variety of issues and through shifts and changes of that line will suffice, prima facie, to support a finding under ¶ 51.135 (*b*).

51.142 *Oath or Affirmation by Applicant as to Membership in Communist Party.* At any stage of the proceedings in the Passport Division or before the Board, if it is deemed necessary, the applicant may be required, as a part of his application, to subscribe, under oath or affirmation, to a statement with respect to present or past membership in the Communist Party. If applicant states that he is a Communist, refusal of a passport in his case will be without further proceedings.

51.143 Applicability of Sections 51.135–51.142. When the standards set out in ¶ 51.135 or ¶ 51.136 are made relevant by the facts of a particular case to the exercise of the discretion of the Secretary under ¶ 51.75, the standards in ¶ 51.135 and 51.136 shall be applied and the procedural safeguards of ¶ 51.137–51.142 shall be followed in any case where the person affected takes issue with the action of the Department in granting, refusing, restricting, withdrawing, cancelling, revoking, extending, renewing, or in any other fashion or degree affecting the ability of a person to use a passport through action taken in a particular case.

For the Secretary of State,
W. K. SCOTT
Acting Deputy Under Secretary

Book Reviews

The Physical Chemistry of Surface Films. William D. Harkins. New York: Reinhold Pub., 1952. 413 pp. $10.00.

The writing of this book was undertaken by Harkins during the last year of his long and busy career as a scientist and teacher. Thanks to the assistance of several devoted former students and associates, the manuscript was completed and edited in less than a year after Harkins' death.

In a brief foreword, P. Debye calls attention to the author's tremendous productivity, experimental skill, and thoroughness. This is followed by an understanding introduction and tribute by Harkins' associate, T. F. Young. Chapters are devoted to "The Nature and Energies of Surfaces," "Films on Liquids," "Films on Solids," "Properties of Soap Solutions," and "Mechanism of Emulsion Polymerization;" the final chapter, contributed at Harkins' invitation by E. J. W. Verwey, concerns "The Role of the Electrical Double Layer in the Behavior of Lyophobic Colloids."

The major portion of the text is made up of numerous sections reproduced almost verbatim from original papers by Harkins and his co-workers or from reviews prepared by Harkins for various journals and books, particularly his relatively recent contributions to Alexander's *Colloid Chemistry* and to Weissberger's *Physical Methods of Organic Chemistry*. New matter in the form of discussions will be found here and there, especially in the chapters concerning films on solids, soap solutions, and emulsion polymerization. The first two chapters are somewhat marred by the use of many unretouched small diagrams taken from early original papers and by printing upside down the figure on page 300.

In many ways the title of this book is misleading. It is not a review of the field indicated by the title, nor is it a treatise on the subject—instead, it is an up-to-date and full review of the contributions to that field by Harkins and his co-workers. It represents Harkins' final evaluation of a lifelong project. Contributions by other investigators are generally referred to or discussed insofar as they illuminate or provide necessary background for understanding or evaluating his work. Hence, classic theoretical contributions on surface tension phenomena by Laplace, Kelvin, Verschaffelt, and Guggenheim are ignored, and basic experimental contributions by Langmuir, Adam, Rideal, Joly, Sugden, Bangham, McBain, and Bowden have either been omitted or given casual mention. The omissions are too numerous to count; as examples, nothing is said of the contributions of Bartell, Powney, McCleod, Trillat, Sebba and Briscoe, and Wenzel.

This volume is not suitable for use as a textbook nor as a general reference for technical workers. It is an incomplete exposition of the subject, its style and organization make it difficult to read, and no one but an expert could read it without getting a most incorrect historical perspective of the subject. Unquestionably, it will be a valuable reference to investigators of surface films and their properties as the best single source of information on the work of Harkins and his many able students and associates. Most important of all, the book is a monument to a scientist whose enthusiasm, meticulous care, and skill in the study of the behavior of surfaces and molecular films brought him world fame.

W. A. ZISMAN
Chemistry Division, Naval Research Laboratory

Progress in Biophysics and Biophysical Chemistry, Vol. 2. J. A. V. Butler and J. T. Randall, Eds. New York: Academic Press; London: Pergamon Press, 1951. 323 pp. $8.00.

International Review of Cytology. Vol. I. Prepared under the auspices of the International Society for Cell Biology. G. H. Bourne and J. F. Danielli, Eds. New York: Academic Press, 1952. 368 pp. $7.80.

There is a world of difference between the two volumes recently published by the Academic Press: *Progress in Biophysics* is exceedingly good, but the *International Review of Cytology* is disappointing. This contrast seems strange when it is realized that biophysics is a relatively narrow category of techniques, whereas cell biology is an extremely broad field underlying almost all paths of biological study. Subject matter, however, is not responsible for the disparity in quality between the two volumes—success and failure would appear to rest largely with the editors of the respective reviews.

From their preface to Volume 1 of *Progress in Biophysics,* it is apparent that Butler and Randall approached their task modestly—and properly so. Contributors were unceremoniously instructed to write critical reviews "which may be read with profit by many who are not experts and which will provide scientists with a general survey of recent work and ideas." In reading Volume 2 it is possible at once to sense the effort that the editors have expended and to appreciate the ably written and properly guided contributions. Of the eight constituent articles two may prove difficult to many biologists. Both Jordan's review of the "Physicochemical Properties of the Nucleic Acids" and Wyke's review of the "Biophysical Aspects of Nervous Function" are, to the nonspecialist, difficult reading. The remaining six, however, are well composed. "Birefringence of Cytoplasm and Cell Membranes," a critical account by Swann and Mitchison, is brief and to the point. Preston has contributed an orderly and understandable treatment of cellulose structure. Pirenne's discussion of the quantum physics of vision is unusually lucid; physical data are explained in terms that are understandable and stimulating to biologists in general. Gray has provided a good general account of the biological action of ionizing radiations, and Wyckoff has ably discussed the electron microscopy of plant and animal viruses. Sinclair and Lamerton's review of the physical principles underlying the use of radioactive isotopes will almost certainly prove valuable to all those concerned—and they are many.

In the preface to the *International Review of Cytology* one learns that the editors are conscious of the broad nature of their field and that they harbor pretentious aims, but one of the principal duties of editorship—to delineate the area of survey with some measure of specificity—is passed off with the vague proposal to keep the scope of the series "as wide as possible." So fine an aim might be welcomed in the case of fields that are loosely defined, but cell biology can easily be conceived to include reviews of enzymology, protein chemistry, biophysics, etc. If it is the objective of the editors to embrace all these allied fields, then this reviewer considers the project nonsensical; if the editors have a more limited and useful plan it remains thus far unknown to the reader, for the first volume reflects little if any planning. It reads like the collected works of a diversified research institute, not like a book designed to serve the needs of cell biologists. It would serve no purpose to appraise each contribution singly, especially since it is the critic's opinion that the deficiencies of many of the articles are in large measure attributable to the editors. A few examples will therefore suffice.

The review of nuclear reproduction by C. L. Huskins is a babel of ideas that warranted presentation at the 1950 Congress of Cell Biology, but not in a solid and reasoned review of progress in the field. Goldacre's account of "The Folding and Unfolding of Protein Molecules as a Basis of Osmotic Work" is an expanded speculation based on a correlation between protoplasmic streaming and dye absorption. Brevity would have done the idea justice, and an enlarged consideration of other approaches to osmotic work would have done the readers a more bountiful service. To be sure, the merits of the articles as such are not in question; what is

here being brought to judgment is the propriety of such articles in a volume designed to serve as a central source of guidance to students of cell biology.

The same lack of direction that runs through the treatment of many subjects is apparent in the choice of topics. Kidder's article on nutritional requirements of *Tetrahymena* would better serve science by appearing elsewhere. Rothschild's brief account of spermatozoan behavior in the neighborhood of eggs certainly adds to the table of contents, but somewhere the editors ought to have drawn a line between what belongs in a current journal and what deserves the status of a review. A striking example is the selection of "The Histochemistry of Esterases" (Gomori) as a topic for review when the fundamental issues of histochemistry, which currently beg for discussion, are neglected. There is hardly a serious student of biology who would not eagerly search for some critical account of this whole field. If the editors are not aware, then they should be, of the multitude of errors that have crept into the literature and that have been uncritically used by many cell biologists. In the face of this, one cannot help wondering with what degree of attention and perspective the editors undertook the important—and admittedly difficult—task of editing a review volume on cell biology.

Happily, the volume contains a number of good reviews. Bell has written a fine account of the application of freezing and drying techniques in cytology. Hershey's review of the reproduction of bacteriophage is beautifully written, and Fankhauser has provided an excellent discussion of nucleo-cytoplasmic relations in amphibian development. Yet the book as a whole is disappointing, and unless future volumes are vastly improved, the series will never serve the purpose for which it was launched.

HERBERT STERN
Rockefeller Institute for Medical Research, New York

Association Affairs

AAAS Symposia at the St. Louis Meeting

Raymond L. Taylor
Assistant Administrative Secretary, AAAS

CHARACTERISTICALLY, AAAS symposia explore relatively neglected areas of scientific inquiry, constitute up-to-date surveys of knowledge in particular fields, or are concerned with the interrelations of science and human welfare. Such programs are significant and valuable because they focus attention upon critical areas, summarize the present status of current research, and provide viewpoints from which to direct further research. In general, these programs originate in the minds of the officers of the eighteen sections and subsections of the AAAS and are developed by them or by others whom they deputize as program chairmen. Often the sectional symposia are concerned with interdisciplinary problems and are sponsored by two or more sections; participating societies also may collaborate. If the potential demand warrants it, the papers are gathered together and published by the Association as symposium volumes.

In recent years the practice has become well established of arranging several symposia of especially wide interest or timeliness for each annual meeting. The responsibility for developing these general symposia, sponsored by the Association as a whole, rests upon a Symposium Committee, appointed each year by the president of the Association. Upon occasion, a proposed sectional program may be chosen to be developed as a general symposium; more commonly, the Symposium Committee, which represents a variety of scientific fields itself, plans and arranges these general sessions. The committee may invoke the aid of consultants and appoint others to implement the general symposia.

The 1952 Symposium Committee consists of Detlev W. Bronk, president of The Johns Hopkins University and of the AAAS (*chairman*); William A. Albrecht, chairman, Department of Soils, University of Missouri; Edgar Anderson, Engelmann professor of botany, Washington University, and assistant director, Missouri Botanical Garden; Arthur H. Compton, chancellor, Washington University; Edward A. Doisy, Sr., director, Department of Biochemistry, Saint Louis University School of Medicine; Charles Allen Thomas, president, Monsanto Chemical Company, and general chairman of the St. Louis Meeting; Carl Tolman, dean, Graduate School of Arts and Sciences, and chairman, Department of Geology, Washington University; John W. Tukey, Department of Mathematics, Princeton University; Clyde E. Williams, director, Battelle Memorial Institute; Conway Zirkle, Department of Botany, University of Pennsylvania; and Raymond L. Taylor (*secretary*).

Of the general symposia at this year's meeting, "Disaster Recovery" was originally proposed by the AAAS Section M Committee; "The Nation's Nutrition" was suggested by Edward A. Doisy, Sr.; and "Applications of the Theory of Games" was conceived and organized by John W. Tukey.

General Symposia

I. Disaster Recovery. Saturday morning and afternoon, Dec. 27. Arranged by Howard A. Meyerhoff.

Part 1. The Nature of Disasters

Lloyd V. Berkner, president, Associated Universities, Inc., *Presiding*

1. The Common Aspects of Disasters. Lloyd V. Berkner.
2. Natural Disasters. James B. Macelwane, dean, Institute of Technology, Saint Louis University.
3. Industrial Disasters. G. M. Kintz, chief, Accident Prevention and Health Division, Region VI, U. S. Bureau of Mines, Dallas.
4. Mine Fires and Explosions. James Westfield, chief, Health and Safety Division, U. S. Bureau of Mines, Washington, D. C.
5. Psychological and Sociological Factors in Disasters. Donald G. Marquis, chairman, Department of Psychology, University of Michigan.

Part 2. Disaster Recovery

Ernest E. Howard, consulting engineer, New York, and Kansas City, Mo., *Presiding*

1. Emergency Measures—the Human Element. Robert C. Edson, assistant national director, Disaster Services in Charge of Rehabilitation, American National Red Cross, Washington, D. C.
2. Emergency Repair of Public Works and Public Utilities. Kenneth M. Kent, Civil Engineer Corps Officers' School, Bureau of Yards and Docks, Department of the Navy.
3. Restoration of Communications. Rudy Eklund, general plant manager, Southwestern Bell Telephone Co., Topeka, Kan.
4. Re-establishment of Transportation. R. P. Hart, chief operating officer, Missouri Pacific Railroad, St. Louis, Mo.
5. Restoration of Community Functions. Frank P. Zeidler, mayor, City of Milwaukee.
6. The Basic Elements in Disaster Recovery. Ernest E. Howard.

II. Applications of the Theory of Games. Monday morning, Dec. 29. Arranged by John W. Tukey.

A. W. Tucker, Princeton University, *Presiding*

1. General Introduction. John von Neumann, Institute for Advanced Study, Princeton, N. J.
2. Conflicts with Imprecise Payoffs. John D. Williams, chief, Division of Mathematics, Rand Corporation, Santa Monica, Calif.
3. Business and Industry. John McDonald, Board of Editors, *Fortune* Magazine, New York

III. The Nation's Nutrition: From Soil to Cytoplasm. Tuesday morning and afternoon, Dec. 30. Arranged by Howard B. Lewis, professor and head, Department of Biological Chemistry, University of Michigan Medical School.

Part 1. Sources of Food.

Howard B. Lewis, *Presiding*

1. Soils and their Relation to Food Production. Lloyd M. Turk, professor and head, Department of Soil Science, Michigan State College.
2. Foods of Plant Origin. George R. Cowgill, professor of nutrition, Department of Physiology, Yale University.
3. The Production of Foods of Animal Origin. Roy C. Newton, vice president in charge of research, Swift & Company.
4. The Deterioration of Food and Foodstuffs. E. C. Stakman, professor and chief, Division of Plant Pathology and Botany, University of Minnesota.

Part 2. Assimilation of Food.

Edward A. Doisy, Sr., *Presiding*

1. General Biochemistry and Health Relationships of Nutrition. C. Glen King, professor of chemistry, Columbia University, and scientific director, Nutrition Foundation, Inc.
2. Protein Requirements of the Diet. James B. Allison, professor of physiology and biochemistry, and director of the Bureau of Biological Research, Rutgers University.
3. Fats and Carbohydrates in the Diet. Harry J. Deuel, Jr., professor of biochemistry and dean, Graduate School, University of Southern California.
4. Vitamins and Minerals. Conrad A. Elvehjem, professor and chairman, Department of Biochemistry, and dean, Graduate School, University of Wisconsin.

Sectional and Society Symposia

B—Physics

Nuclear Science in Industry; arranged by Ralph T. Overman.

Research Applications of Carbon 14; arranged by Ralph T. Overman.

Magnetic Resonance and its Applications; arranged by Arthur L. Hughes.

Tornadoes and Tornado Forecasting; arranged by Edward M. Brooks.

C—Chemistry

The New Synthetic Fibers (two sessions); arranged by Frank J. Soday.

Contributions of Chemistry in the Field of Human and Animal Nutrition (two sessions); arranged by Barrett L. Scallet.

Contributions of Chemistry to Medicine; arranged by Kenneth N. Campbell.

Chemistry and Dentistry Team Up for Progress (two sessions); arranged by Frances Krasnow.

Contributions of Chemistry to the Cancer Problem; arranged by Kenneth N. Campbell.

Liquid Fuel Supplies of the Future and the Impact on the Chemical Industry of Chemicals Available as Co-products from Synthetic Fuel Processes (two sessions); arranged by L. L. Hirst.

Contributions of Chemistry to Agriculture (two sessions); arranged by Lloyd V. Sherwood.

E—Geology and Geography

Modern Research of State Geological Surveys and its Economic Values (two sessions); arranged by M. M. Leighton.

F—Zoological Sciences

The six following programs were all arranged by R. E. Blackwelder

Public Book Discussion Panel: *Time's Arrow and Evolution.*

Public Book Discussion Panel: *The Meaning of Evolution.*

Life History Studies in Relation to Systematics.

Anecdotal Sketches of Famous Zoologists.

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Public Book Discussion Panel: *Three College Zoology Texts.*

G—Botanical Sciences

Improvement in the Teaching of Taxonomy; arranged by Aaron J. Sharp.

Biosystematics and Taxonomic Units; arranged by Edgar Anderson.

Nitrogen Metabolism in the Green Plant (two sessions); arranged by Barry Commoner.

The Western Range—Our Great Natural Resource; arranged by F. W. Albertson and David F. Costello.

Plant Sociology and the Taxonomy of Vegetational Units (two sessions); arranged by Stanley A. Cain.

H—Anthropology

The Plains and the Rio Grande Pueblos; arranged by James B. Watson.

I—Psychology

Men and Machines (two sessions); arranged by Philip H. DuBois.

Problems in Psychotherapy; arranged by Robert I. Watson.

K—Social and Economic Sciences

Social and Economic Aspects of Technical Assistance Programs (three sessions); arranged by Conrad Taeuber and Gordon Macgregor.

Information Processing in Social and Industrial Research; arranged by Amos E. Taylor.

Regional Research: Emerging Concepts and Techniques; arranged by Walter Isard.

The Individual Scientist in Today's World; arranged by Franklin Miller, Jr.

L—History and Philosophy of Science

Relations between Science and Thomistic Philosophy; arranged by Raymond J. Seeger.

Methodology of Engineering Research; arranged by Raymond J. Seeger.

Leonardo da Vinci; arranged by Raymond J. Seeger.

Philosophical Problems of Contemporary Biology; arranged by Henry Margenau.

Confirmation of Scientific Theories; arranged by Henry Margenau.

M—Engineering

Hearing and Speech Aids; arranged by Eugene F. Murphy.

N—Medical Sciences

Survival of Frozen Tissues, Normal and Tumors (two sessions); arranged by B. J. Luyet.

Nm—Medicine

Fluid and Saline Therapy; arranged by Carl A. Moyer.

Chemotherapy of Tuberculosis; arranged by Alfred Goldman.

The Social Sciences and Humanities in Medical Education; arranged by Hugh E. Setterfield.

Industrial Hygiene: An Applied Science; arranged by Elmer P. Wheeler.

Health Hazards and Health Protection (three sessions); arranged by Gordon K. Moe.

Nd—Dentistry

The Chemistry of Saliva; arranged by F. J. McClure and Isadore Zipkin.

Scientific Contributions to the Manufacture of Restorative Dental Materials; arranged by Floyd A. Peyton.

Engineering and Chemical Factors of Water Fluoridation; arranged by A. P. Black.

Np—Pharmacy

Programs arranged by George F. Archambault

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Content of Hospital Pharmacy Courses in Schools of Pharmacy.

The Role of the USP, the NF, the NNR, and the ADR in Developing and Maintaining Sound Drug Therapy Trends and Standards.

Medical Societies

Problems in Forensic Sciences (two sessions); arranged by Ralph F. Turner and R. B. H. Gradwohl.

Science and Medical Care; arranged by E. M. Bluestone.

Education in Physiological Science (two sessions); arranged by Maurice B. Visscher, H. Burr Steinbach, and Orr Reynolds.

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Effective Utilization of Industrial Manpower (two sessions); arranged by Allen T. Bonnell.

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Identification of Talented Youth in Science and Mathematics; arranged by Morris Meister.

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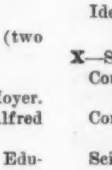

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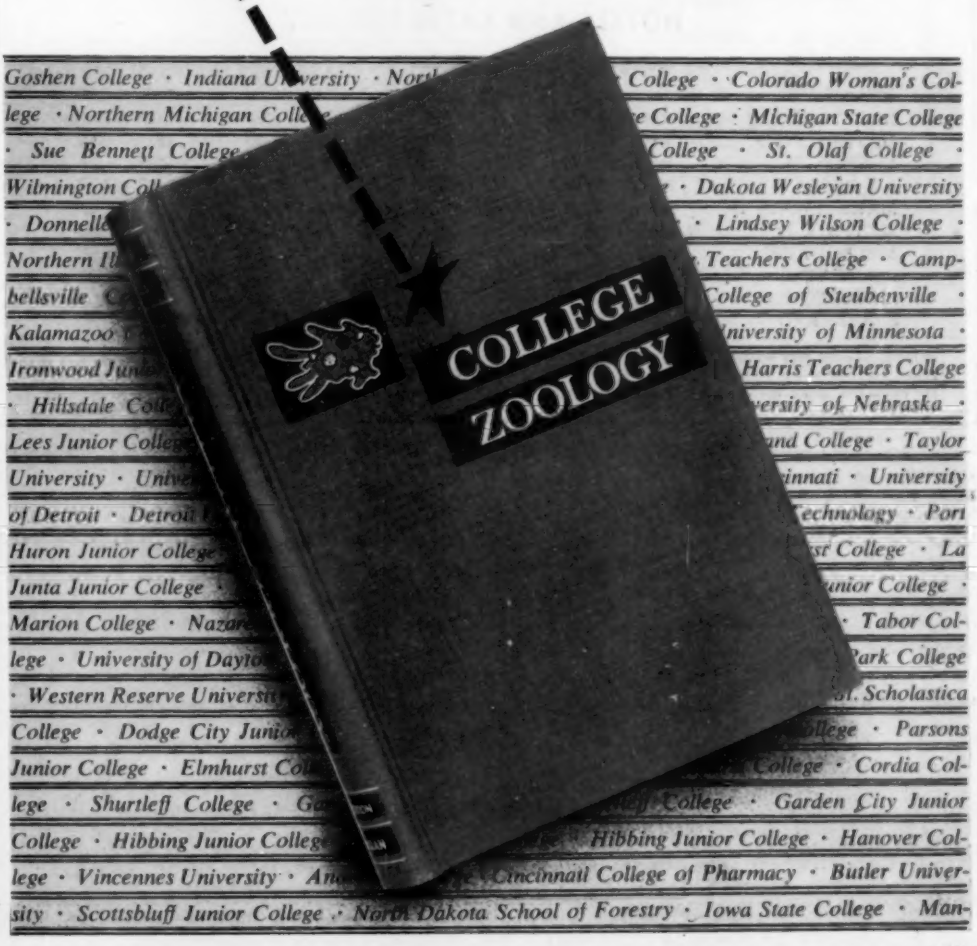

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Australian Arthrodires. Vol. 1, No. 9. Errol White. 55 pp. Illus. 15s.; ***A Revision of the West Indian Species of Selaginella. A New Species of Cheilanthes from Africa and Some Additions to the Fern Flora of Northern Rhodesia.*** Vol. 1, No. 2. A. H. G. Alston. 49 pp. + 2 plates. 8s.; ***A Catalogue of the American Hesperiidae in the British Museum (Natural History),*** Part II. ***Pyrginae,*** Sec. 1. W. H. Evans. 178 pp. + 25 plates; ***The Miocene Lemuroids of East Africa. The Fossil Mammals of Africa,*** No. 5. W. E. Le Gros Clark and D. P. Thomas. 20 pp., 3 plates. 12s.6d. London: British Museum (Natural History), 1952.

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Tables of the Bessel Functions $Y_0(x)$, $Y_1(x)$, $K_0(x)$, $K_1(x)$, $0 \leq x \leq 1$. National Bureau of Standards Applied Mathematics Ser. 25. Washington, D. C.: GPO, 1952. 60 pp. 40¢.

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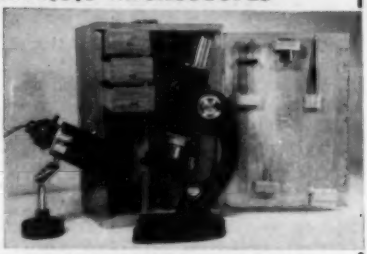

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Nov. 13–15. Geological Society of America. Hotel Statler, Boston.

Nov. 15. Symposium on Cerebral Palsy, United Cerebral Palsy Associations. New York Academy of Medicine, New York.

Nov. 17–19. Association of Military Surgeons of the United States. Hotel Statler, Washington, D. C.

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Nov. 17–21. Soil Science Society of America. Netherland Plaza Hotel, Cincinnati.

Nov. 18–19. Building Research Advisory Board. Conference on Housing and Building in Hot-Humid and Hot Dry Climates. National Academy of Sciences, Washington, D. C.

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Nov. 19. Institute of Metals Symposium on Properties of Metallic Surfaces. Royal Institution, London.

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Nov. 19–21. National Fertilizer Association (Annual Fall). Roney Plaza Hotel, Miami Beach.

Nov. 20–21. Corrosion Conference, National Association of Corrosion Engineers, Western Region. Biltmore Hotel, Los Angeles.

Nov. 20–22. Mineralogical Society of America. Hotel Statler, Boston.

Nov. 20 and Dec. 12. Association of Vitamin Chemists. Illini Union Bldg., Chicago.

Nov. 21–24. International Congress on Hydatid Disease. Santiago, Chile.

Nov. 24–25. Conference on Electronic Instrumentation and Nucleonics in Medicine (Annual). American Institute of Electrical Engineers. Hotel New Yorker, New York.

Nov. 25. American Standards Association (Annual). Waldorf-Astoria Hotel, New York.

Nov. 28–29. American Mathematical Society (Southeastern). University of North Carolina, Raleigh.

Nov. 28–29. American Mathematical Society (Western). Purdue University, Lafayette, Ind.

Nov. 28–29. American Physical Society. Washington University, St. Louis.

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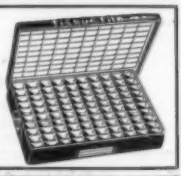

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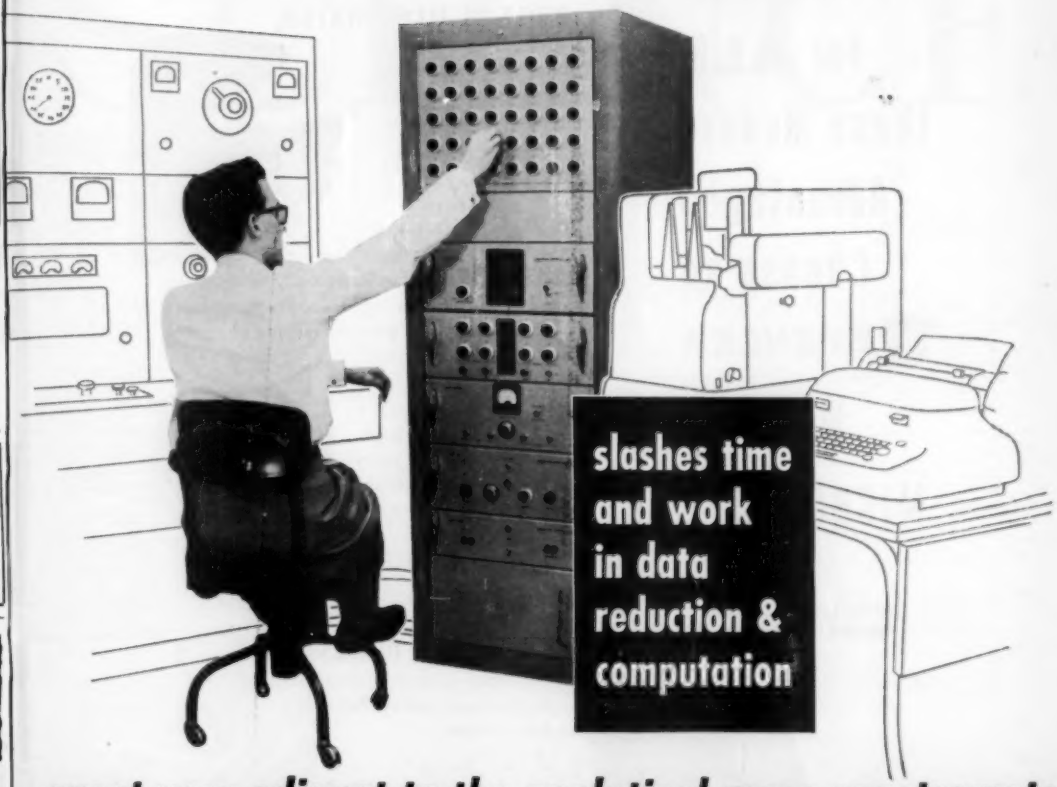

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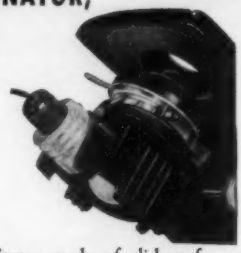

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